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The Environmental Lead Problem An Assessment of Lead in Drinking Water from a Multi-Media Perspective

MITRE Corp, McLean, VA METREK Div

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THE ENVIRONMENTAL LEAD PROBLEM: AN ASSESSMENT OF LEAD IN DRINKING WATER FROM A MULTI-MEDIA PERSPECTIVE

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

MAY 1979

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Human exposure to lead has been shown to be cumulative in nature. In order to assess the toxicological significance of environmental lead exposures, it is necessary to define the contributions to an individual's daily lead uptake from all possible exposure pathways. This paper defines and quantifies the major environmental sources of lead exposure, describes the absorption characteristics of lead compounds in man via each exposure route, determines the source contribution factors for daily lead uptake by each exposure pathway, and relates those contributions to an individual's blood-lead level.

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ABSTRACT

Human exposure to lead has been shown to be cumulative in nature. In order to assess the toxicological significance of environmental lead exposures, it is necessary to define the contributions to an individual's daily lead uptake from all possible exposure pathways. This paper defines and quantifies the major environmental sources of lead exposure, describes the absorption characteristics of lead compounds in man via each exposure route, determines the source contribution factors for daily lead uptake by each exposure pathway, and relates those contributions to an individual's blood-lead level.

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EXECUTIVE SUMMARY

The MITRE Corporation/Metrek Division has been assisting the Criteria and Standards Division, Office of Drinking Water, in their assessment of the adequacy of the current interim standard for lead (Pb) in drinking water. In this assessment, the biological effects of lead exposure are reviewed, the major environmental sources of lead exposure (air, food, drinking water, soil/dust and paint) are quantified, the sensitive populations are identified and a relationship between exposure levels and blood-lead levels is developed.

The method employed in this study is to estimate the degree to which each major environmental source of lead exposure contributes to an individual's total daily lead uptake, based on probable exposure conditions (i.e., ambient lead levels) as well as individual biological absorption rates for each exposure route. These source contribution factors (percent contribution from each source to total daily lead uptake) identify the relative significance of each source in producing overall toxic consequences, and thus point out those areas where regulatory action will have the greatest effect.

Since the blood-lead level is the value most widely reported in the literature to represent the extent of lead absorption, it is necessary to relate daily lead uptake to blood-lead values in order to define the toxicological impact associated with different levels of lead uptake.

Environmental Lead Sources

Lead is a natural constituent of the earth's crust, but the presence of lead in the remainder of the environment is the result of extensive human use of lead. The chemical properties associated with the more common forms of lead result in low lead levels in natural waters.

The majority of lead compounds found in the atmosphere result from leaded gasoline combustion. In 1975, the most recent year for which data are available, approximately 88.8 percent of the total atmospheric lead arose from this emission source. The next largest contributors, primary copper and lead smelting facilities, provided 2.5 and 1.7 percent of the total. Localized atmospheric lead pollution resulting from industrial plants processing lead and its products can be quite severe, but the contribution of these plants to the pollution load across large areas is minimal.

The ingestion of foodstuffs containing lead appears, on the average, to be the largest contribution to an adult's total daily lead intake. The source of lead in various foodstuffs may be natural bioaccumulation, deposition of airborne lead particles, or food processing and serving.

Lead concentrations in finished drinking water collected at 969 public water supply systems in the United States ranged from an undetectable amount to 640 micrograms per liter (μg/l). Of the supply systems sampled, 37 sites (1.4 percent of the total) contained lead in concentrations exceeding the current national interim primary drinking water standard of 50 μg/l. Tap water tends to contain higher lead concentrations than water in distribution systems due to the use of lead pipe or lead-containing solder in home plumbing systems.

Soil and dust contain a high concentration of deposited lead particulates. Normal hand-to-mouth activity of children may lead to ingestion of high concentrations of lead compounds, which are then subject to absorption by the gastrointestional tract. Lead levels in soil and dust in metropolitan areas have been reported as high as 12,000 μg/g. Leaded gasoline is the main contributor to these high lead levels.

Lead-containing materials (e.g., paint, plaster, newsprint) are ingested by some children suffering from pica. Extremely high lead concentrations are found in the paint of some on older dwellings.

Toxicologic Properties

Environmental lead compounds can be absorbed into the bloodstream from the lung after inhalation, from the gastrointestional tract after ingestion, or to a limited extent, from direct dermal contact. The absorption kinetics for each of these pathways are dependent upon a number of factors, including the physical and chemical nature of the lead compounds at the time of exposure and the presence of other modifying agents. Once inorganic lead is absorbed into the bloodstream, it is readily transported throughout in the body and does not normally retain any characteristics associated with its exposure or absorption route.

Lead is present in virtually every organ of the human body. Over 90 percent of the lead stored in the adult body is located in the skeleton. Lead concentrations in the majority of soft tissues apparently reach an equilibrium level during the second decade of life and remain at this level indefinitely. Concentrations in the bones, aorta, liver, lungs, kidneys, pancreas and spleen continue to increase with age.

In adults, approximately 90 percent of ingested lead is eliminated in the feces without prior gastrointestinal absorption. Absorption of lead via the gastrointestinal tract is greater in children, who therefore eliminate a substantially smaller proportion of their total intake as unabsorbed lead in the feces. The primary elimination route for lead absorbed by all routes is in the urine, representing about 95 percent of the total output of absorbed lead.

The toxicological impact of lead is the cumulative result of exposure from many sources. Adverse health effects may result from continuous low-level exposure from the ambient environment. Toxic effects are essentially due to the mobile fraction of absorbed lead within the body. This mobile fraction is composed of lead from any recent exposure, as well as the background level of easily mobilized lead previously deposited in the soft tissues and soft (trabecular) bone, and to a lesser extent, to that portion mobilized from dense bone.

Lead inhibits the synthesis of hemoglobin at several points throughout the heme synthetic pathway. The inhibition of the enzyme aminolevulinic acid dehydratase (ALAD) is believed to be the earliest known biological effect of lead intoxication. Anemia is often the earliest clinical sign of chronic and acute lead poisoning. This anemia is believed to be the result of decreased erythrocyte production and increased destruction due to the interference of lead.

Accumulation of lead in the body can lead to severe effects on the central nervous system. These central nervous system effects are most responsible for the morbidity and mortality associated with lead poisoning. Symptoms of neurological changes include ataxia (muscular coordination failure), clumsiness, weakness, stupor, coma and convulsions. There is a great deal of controversy concerning the subtle neurobehavioral effects of low-level lead exposure in asymptomatic humans.

In addition to the effects on the central nervous system, peripheral neuropathy due to lead poisoning has been reported. Peripheral nervous system paralysis is characterized by selective involvement of motor neurons and is manifested as weakness of the extensor muscles.

There appear to be two distinct renal effects from chronic lead exposure, reversible proximal tubular damage and progressive, irreversible renal failure. Although dose-response relationships have not been defined, it appears that the effects occur only at levels above those which affect heme synthesis.

There are many tests which can be used for the detection of increased lead absorption. Tests which measure both tissue lead content and tissue metabolic effects are available. However, no single test can be used for the determination of total body burden or overall metabolic effects. At present, blood-lead concentration is the most widely used measure of tissue lead content.

Two subgroups within the general population have been identified as being more sensitive and at greater risk to environmental lead exposure. Due to many factors, children under the age of four are especially susceptible to the toxic effects of lead. The fetus has also been identified as a lead-sensitive individual, due to the immature state of development of certain organs. Because transplacental absorption is the major source of prenatal lead exposure, the pregnant female must be recognized as the exposure vehicle for the fetus. The blood-lead level in the fetus is approximately the same as that in the mother. Separate lead-uptake-to-blood-lead relationships have been derived for children and pregnant women.

The Center for Disease Control (CDC) set the blood-lead level of significant danger to children at 30 μg/dl. The level of 30 μg/dl set by the CDC is endorsed by the American Academy of Pediatrics and is now the target level defined by EPA as the level of undue lead exposure.

Results

To evaluate the adequacy of the interim primary drinking water standard for lead, it is necessary to predict the blood-lead levels associated with various concentrations of lead in drinking water for identified sensitive populations, and to determine the extent to which altering the maximum allowable concentration of lead in drinking water may affect these populations.

Through the combined use of the derived lead-uptake-to-blood-lead relationship and percent contribution values from the source contribution model, the relationship between various water-lead exposures and resulting blood-lead values can be drawn. The source contribution model represents any specific subunit of the total population by incorporation of the assumed characteristic exposure concentrations and physiologic factors associated with that subunit.

The model has been applied to four hypothetical populations: adult males, pregnant females, nonpica children, and children with pica for paint. Source contribution factors and blood-lead levels in these populations have been calculated using the model. They are described in the following paragraphs.

The range of source contribution factors can be quite large, if one considers all the possible permutations of lead levels in the various media. In pregnant females, the source contribution factor for drinking water varies from about 6 to 70 percent. In children without pica, drinking water contributes between 2 and 74 percent of the daily lead uptake. For the child with pica for paint, drinking water contributes between 1 and 69 percent, depending on the concentration of lead in soil/dust and paint.

Analysis of the effect of varied water-lead intakes in reference to the critical threshold level of 30 µg/dl chosen by EPA and CDC reveals that urban children are the sensitive subgroup. Although water may comprise as much as 42 percent of the source contribution in rural children without pica who are exposed to lead in drinking water at the current standard, their total blood-lead level (12.3 µg/dl) is well below the critical threshold level. Urban children without pica, at the current drinking water standard and above, all display blood-lead values equal to or exceeding the critical threshold level. Urban children with pica for paint (with lead-containing paint at the current standard) display blood-lead levels of 30 µg/dl at water-lead levels below the standard, and blood-lead values well above the critical threshold level at water-lead levels above the standard. Urban children with pica (with lead-containing paint above the standard) display blood-lead levels well above the critical level at all water-lead levels.

At the current water standard, water lead represents 8.5 and 8.2 percent of the total source contribution for urban children without pica and urban children with pica (lead-containing paint at the standard), respectively. In children with pica for paint exposed to lead-containing paint above the standard (8000 µg/g), water contributes 5.8 percent of the total daily lead uptake. Lowering the water-lead concentration from 50 to 10 µg/l produces a decrease in the percent contribution of water lead to total daily lead uptake from 5.8 to 1.2 percent, and a decrease in blood lead from an estimated 40.3 to 38.8 µg/dl.

The blood-lead values of urban pregnant women at an air standard of 1.5 µg/m^3 vary only by 2.7 µg/dl from blood-lead values of pregnant rural women. The blood-lead level of these urban women at the current water standard is estimated to be 16.8 µg/dl, well below the 30 µg/dl level agreed on by EPA and CDC. The percent contribution of water to total lead uptake in urban women ranges from 6.4 percent (at 10 µg/l) to 25.5 percent at the standard (50 µg/l). The blood-lead level in those women varies by about 1.8 µg/dl (i.e., from an estimated 15.0 to 16.8 µg/dl) over this same range of water-lead concentrations.

Blood-lead levels of U.S. children have been characterized as log-normally distributed, with a geometric standard deviation (GSD) of between 1.3 and 1.5 (EPA, 1978). Given the 30 μg/dl threshold level. One can identify the percent of the exposed population with blood-lead levels below 30 μg/dl given a geometric mean blood-lead level. Or, if a selected percentage of the population is to be protected (as a safety margin), one can determine the particular geometric mean which will insure that that percentage will not exceed 30 μg/dl. This statistical treatment allows one to define the extent to which the "tails" of the frequency distribution extend beyond a particular blood-lead level.

More than 99 percent of rural children without pica or with pica at low paint-lead levels, and all female adults are expected to fall below the 30 μg/dl blood-lead guideline, given drinking water lead at the current interim standard of 50 μg/dl. Decreasing drinking water-lead levels for these groups would have a negligible impact, since most individuals within these groups are already below the threshold. A larger proportion of the urban child population exceeds that 30 μg/dl blood-lead level, but the drinking water contribution is only a small fraction of their total daily lead uptake. Assuming drinking water lead at 50 μg/l, between 43.2 and 88.6 percent of the urban child population is expected to have blood lead in excess of 30 μg/dl (see Table 9-1). By reducing the lead level in drinking water to 10 μg/l, between 41.4 and 84.5 percent would exceed the 30 μg/dl threshold.

The complete elimination of water lead from the uptake of the urban child yields an estimated mean blood-lead level of 28.1, 28.9, and 38.4 μg/dl for children without pica, with pica for paint at low paint-lead concentrations, and with pica at high paint-lead concentrations, respectively. The corresponding percentages of the population falling below 30 μg/dl are 64.1, 61.0, and 17.0, respectively. Therefore, the total elimination of water lead in these groups adds 1.5 percent of the population to that portion already below the 30 μg/dl guideline. The effect upon the fetal population of reducing the water-lead standard is not as clearly defined by these manipulations, since the blood-lead levels of the vast majority of the female population are already below 30 μg/dl.

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1.0 INTRODUCTION

The Office of Drinking Water (ODW) within the U.S. Environmental Protection Agency (EPA) in accordance with the Safe Drinking Water Act as amended has promulgated National Interim Primary Drinking Water Regulations for a number of physical, chemical, biological and radiological contaminants in potable water systems. These interim standards, which specify maximum contaminant levels (MCLs) for substances in drinking water, will be replaced by final Primary Drinking Water Regulations as more definitive information describing the health risks associated with each contaminant is accumulated and analyzed.

The MITRE Corporation, Metrek Division has assisted the Criteria and Standards Division, Office of Drinking Water, in their assessment of the adequacy of the current standard for lead (Pb) in drinking water (50 μg/l). As part of this effort, MITRE has defined and quantified the major environmental sources of lead exposure, devel-oped estimates of total daily lead uptake in sensitive subgroups of the general population, defined blood-lead levels resulting from the major environmental sources of exposure, and assessed the public health significance of various levels of lead in drinking water.

1.1 Background

Lead is ubiquitous in the environment and humans are exposed in many ways. Lead in air can be traced to both stationary and mobile (e.g., automobiles) emission sources. Lead occurs naturally in water systems, but a substantial portion of the lead present in drinking water at the household tap is added in the water treatment and distribution processes. Lead also occurs naturally in trace quantities in various foods, but most of the lead in food is attributable to processing and handling. Children are exposed to additional sources of lead in soil/dust and other lead-containing nonfood materials. Both children and pregnant females have been identified as subgroups within the general population that are at greater risk from lead exposure than the remainder of the population.

Lead accumulates in the human body--the majority in the bone, kidney and liver. Lead that has been stored in body compartments can be remobilized long after the initial absorption and produce adverse health effects. Even though the physiological effects of lead have been well-documented, there is still controversy surrounding tolerable blood-lead levels and the significance of environmental sources of lead exposure. Because of the multiple pathways for lead exposure and the cumulative nature of lead exposure, it is necessary to take into account all the lead to which an individual is exposed when considering the implications of a lead drinking water standard. Occupational exposure, however, will not be discussed in this report.

1.2 Approach

In order to properly assess the health significance of lead-contaminated drinking water, it is necessary to define an individual's total daily lead uptake from all sources, to assess the health impacts associated with that total daily uptake and to identify that proportion of the total daily uptake arising from the ingestion of drinking water. In this assessment the following steps were followed:

- Quantify the major environmental sources of lead exposure.
- Determine the absorption/retention/elimination characteristics of those lead compounds commonly found in the environment.
- Develop estimates of total daily lead uptake in man based on ambient exposure levels and absorption/retention characteristics.

- Define the toxicological impacts associated with lead exposure, especially the low level chronic effects for the identified sensitive populations.
- Assess the public health significance of various levels of lead in drinking water, given ambient lead contamination in other environmental media.

The degree of exposure to lead in the environment varies substantially, and is dependent not only upon environmental factors (e.g., lead concentrations in water) but also on individual host characteristics (e.g., age, dietary status). An individual's body lead burden reflects his or her own exposure situation, which often cannot be approximated by "national average" lead concentrations in some medium. Such inherent variability has led MITRE/Metrek to develop a source contribution model that identifies and quantifies the effects of various environmental sources of lead exposure on an individual's blood-lead level. This model permits one to examine all significant sources of lead exposure, and to define the change in blood lead as a result of any changes in exposure characteristics. In this way, various regulatory scenarios can be applied to the environmental lead problem, and thereby aid in the selection of the most cost-effective control option, based on incremental reduction in a population's blood-lead level. This document describes the development of the source contribution model, and applies specifically to the health impacts of lead in drinking water.

2.0 ENVIRONMENTAL SOURCES OF LEAD EXPOSURE

Lead is a natural constituent of the earth's crust, but the presence of lead in the remainder of the environment is mainly the result of extensive use of lead and lead compounds by man. The chemical properties of the more common forms of lead result in low lead levels in natural waters.

Because the toxicological effects associated with lead exposure can be considered cumulative, it is imperative to define and quantify all major sources of human lead exposure. Ambient air, food, and drinking water are the major sources of exposure for adults, while soil and dust, via normal hand-to-mouth activity, and various lead-containing materials via pica* are significant additional sources of exposure for children. Inhalation and ingestion of lead-containing substances by adults and children appear to be the predominant routes of exposure, although dermal absorption may be significant in certain instances.

Humans are exposed to lead and lead-containing compounds through the various environmental pathways illustrated in Figure 2-1. In the following sections, and in later chapters, the occurrence of lead in the major exposure pathways is exemplified, and lead levels in the significant exposure media that are representative of an average or range of hypothetical exposure conditions for selected populations are derived from the literature.

2.1 Lead Concentrations in Ambient Air

The majority of lead compounds found in the atmosphere result from leaded gasoline combustion. In 1975, the most recent year for which data are available, approximately 88.8 percent of the total atmospheric lead arose from that emission source. The next largest

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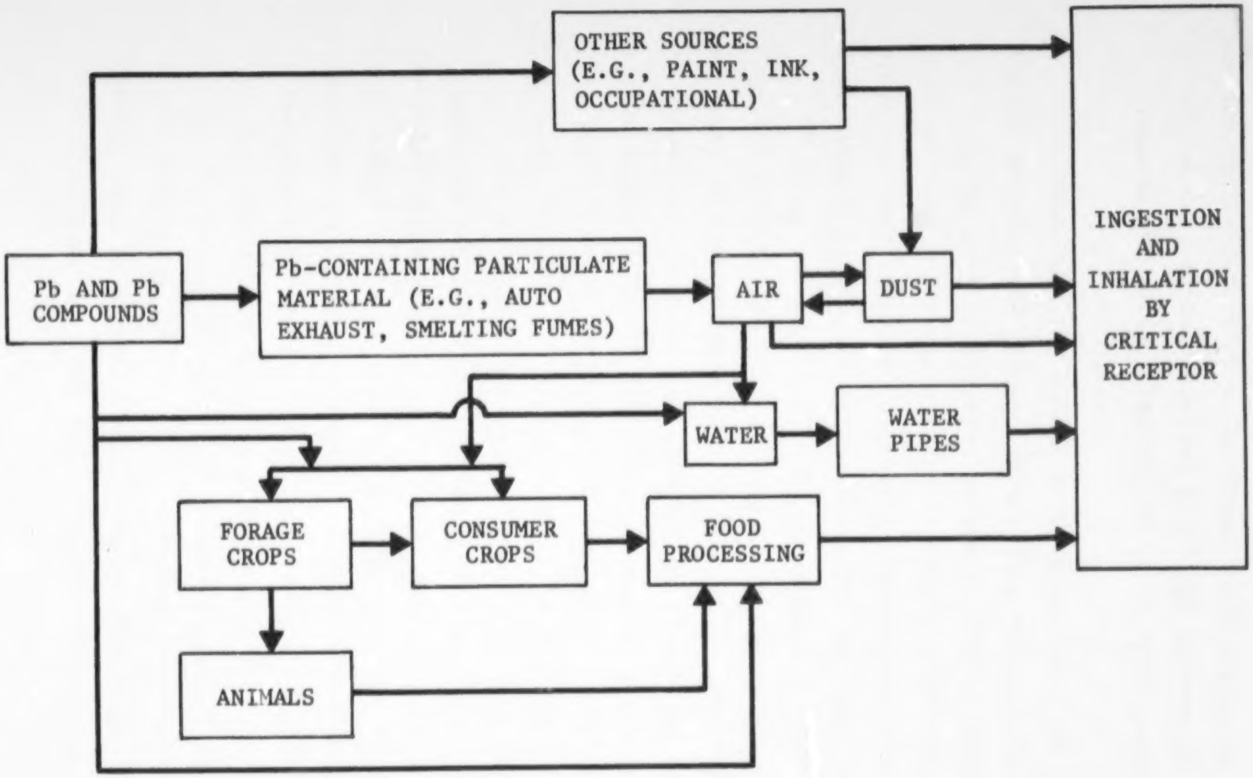
*The ingestion of nonfood material.


OTHER SOURCES (E.G., PAINT, INK, OCCUPATIONAL)
Pb AND Pb COMPOUNDS
Pb-CONTAINING PARTICULATE MATERIAL (E.G., AUTO EXHAUST, SMELTING FUMES)
AIR
DUST
INGESTION AND INHALATION BY CRITICAL RECEPTOR
WATER
WATER PIPES
FORAGE CROPS
CONSUMER CROPS
FOOD PROCESSING
ANIMALS

SOURCE: Adapted from Jenkins, 1976

FIGURE 2-1
MAJOR ENVIRONMENTAL LEAD EXPOSURE PATHWAYS

contributors, primary copper and lead smelting facilities, provided 2.5 and 1.7 percent, respectively, of the total (EPA, 1978a). Local atmospheric lead pollution from industrial plants processing lead and its products can be severe, but their overall contribution to the pollution load across large areas is minimal (Atkins and Krueger, 1968).

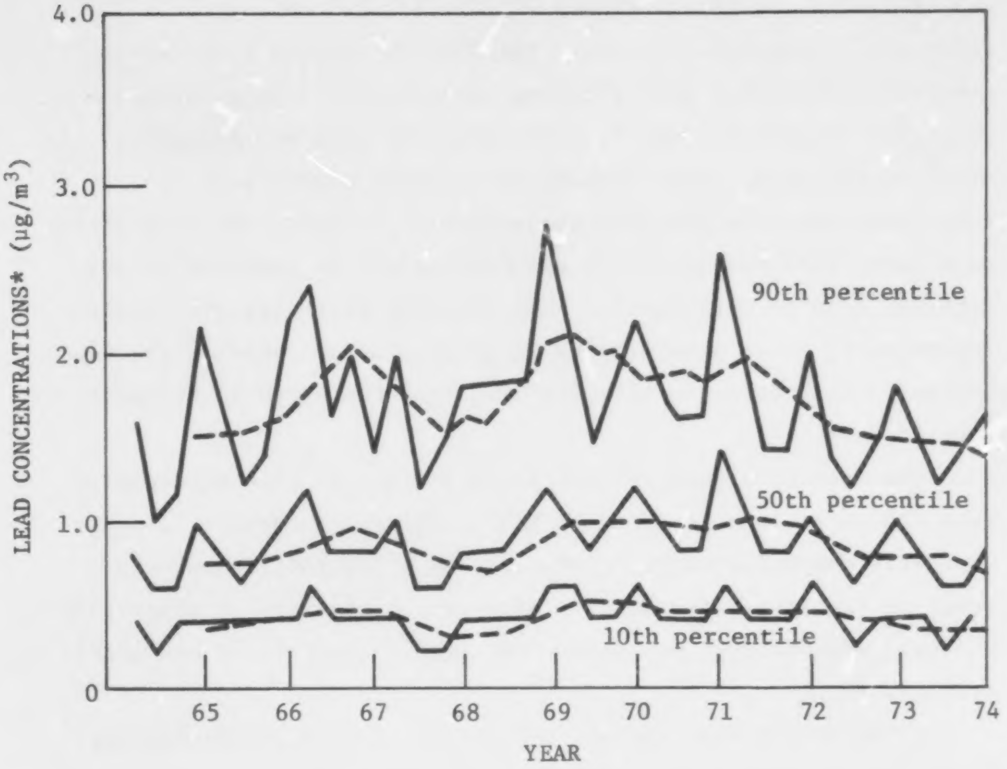
The National Air Sampling Network (NASN) has routinely collected and analyzed airborne particulate samples for selected metals since the early 1960s. Their sampling protocol (Hi-vol filter samples) defines the total suspended particulate (TSP) material in ambient air. Recent studies have indicated, however, that the atmospheric lead constituent of TSP is comprised of particles whose mass median diameter (MMD) is approximately 0.2 to 1.43 μ. Up to 74 percent of the particles are less than 1 μ in diameter (Lee and von Lehmden, 1973; Harrison, 1973). It is widely believed that particles in this size range are easily respirable, and reach the innermost parts of the lung, since pulmonary deposition of inhaled particulate matter is greatest in the 0.01 to 2 μ range (Task Group on Lung Dynamics, 1966). Virtually all lead deposited in the lung is eventually absorbed into the blood (Kehoe, 1961; NAS, 1972).

In addition to inorganic lead particulate material, the atmosphere may contain organic lead vapors (e.g., lead alkyls) which are not detected by NASN sampling protocols. Most of these organic lead compounds arise from the production, handling, and use of gasoline containing lead anti-knock additives. They are photoreactive and their presence in local atmospheres is transitory. Studies have indicated that lead alkyls represent less than 10 percent of the total lead loading in the atmosphere (NAS, 1972). Therefore, any health hazard associated with organic lead exposure is most likely to occur in an occupational setting (e.g., gasoline handling operations).

According to NASN data, the levels of lead compounds in the atmosphere are slowly decreasing, mainly as a result of the decreased use of leaded gasoline. Figure 2-2 illustrates this gradual reduction in atmospheric lead. The data in Table 2-1 represent cumulative frequency distributions of atmospheric lead for all quarterly results by year at both urban and nonurban locations. As might be expected, urban atmospheres contain higher lead concentrations than nonurban atmospheres. In 1974, the arithmetic mean urban lead concentration was 0.89 $\mu g/m^3$, as compared to the nonurban mean of 0.11 $\mu g/m^3$. When nonurban locations are classed according to their proximity to large population centers, the lead concentrations decrease with distance from the urban environment, as seen in Table 2-2.

The data in Figure 2-2 and Table 2-1 are average atmospheric lead concentrations reported by NASN. The data represent average quarterly composite samples taken at 300 urban and 35 nonurban sampling stations nationwide. There can be substantial geographical, diurnal, and seasonal variations not readily evident in the yearly averages data.

Although the NASN annual averages are useful in identifying trends in air-lead levels, one should examine data from individual sampling sites or regional areas to identify those locations that experience higher than average lead concentrations. For example, the NASN data for the Burbank, California, sampling station indicate yearly averages ranging from 2.46 to 4.93 $\mu g\ Pb/m^3$ between 1970 and 19[illegible]. In the same period, sampling in Los Angeles indicated an ambient lead concentration (yearly average) ranging from 2.12 to 4.63 $\mu g/m^3$ (Akland, 1976).



*Ninetieth percentile indicates that 90 percent of all NASN stations reporting showed lead concentrations at or below the particular value.

SOURCE: Faoro and McMullen, 1977

FIGURE 2-2
SEASONAL PATTERNS AND TRENDS IN QUARTERLY AVERAGE URBAN LEAD CONCENTRATIONS (NASN DATA)

TABLE 2-1

AVERAGE AMBIENT ATMOSPHERIC LEAD CONCENTRATIONS:
QUARTERLY COMPOSITES ($\mu g/m^3$)

Location	Year	Number Stations	Minimum Reported Value	Cumulative Frequency Distributions							Maximum Reported Value	Arithmetic	
				10	30	50	70	90	95	99		Mean	Standard Deviation
Urban	1970	797	ND*	0.47	0.75	1.05	1.37	2.01	2.59	4.14	5.83	1.19	0.80
	1971	717	ND	0.42	0.71	1.01	1.42	2.21	2.86	4.38	6.31	1.23	0.87
	1972	708	ND	0.46	0.71	0.97	1.25	1.93	2.57	3.69	6.88	1.13	0.78
	1973	559	ND	0.35	0.58	0.77	1.05	1.62	2.08	3.03	5.83	0.92	0.64
	1974	594	0.08	0.36	0.57	0.75	1.00	1.61	1.97	3.16	4.09	0.89	0.57
Nonurban	1970	124	0.003	0.003	0.003	0.003	0.003	0.267	0.383	0.628	1.471	0.088	0.190
	1971	85	0.003	0.003	0.003	0.003	0.003	0.127	0.204	0.783	1.134	0.047	0.155
	1972	137	0.007	0.007	0.007	0.107	0.166	0.294	0.392	0.950	1.048	0.139	0.169
	1973	100	0.015	0.015	0.015	0.058	0.132	0.233	0.392	0.658	0.939	0.110	0.149
	1974	79	0.007	0.007	0.053	0.087	0.141	0.221	0.317	0.496	0.534	0.111	0.111

---

[*] Not detected

SOURCE: Adapted from Akland, 1976.

Example: In 1974, urban lead concentrations averaged 0.89 $\mu g/m^3$, with a maximum reported quarterly value of 4.09 $\mu g/m^3$; for 1974, 95% of the reported lead concentration were $\leq$ **1.97 $\mu g/m^3$**.

TABLE 2-2

ATMOSPHERIC LEAD GRADIENTS ASSOCIATED WITH URBANIZATION*

	Urban	Nonurban		
		Proximate	Intermediate	Remote
Number of stations reporting	217	5	15	10
Lead concentration	1.11 $\mu g/m^3$	0.21 $\mu g/m^3$	0.096 $\mu g/m^3$	0.022 $\mu g/m^3$

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[*] 1966-1967 NASN data

SOURCE: Adapted from McMullen et al., 1970

In 1974 and 1975, there were fifty-six Air Quality Control Regions (AQCRs)* that reported a lead concentration in excess of 1.5 $\mu g/m^3$ in at least one quarterly composite sample (Preston, 1977). The maximum quarterly lead concentration of 32.0 $\mu g/m^3$ was reported for the northern Idaho/eastern Washington AQCR. Over 50 percent of its samples indicated lead at concentrations equal to or greater than 4 $\mu g\ Pb/m^3$. These atmospheric lead measurements were substantiated by other unrelated monitoring surveys during the same period, which reported annual average lead concentrations ranging from 0.5 to 23 $\mu g/m^3$ in the same geographical area (Yankel et al., 1977; Idaho Department of Health and Welfare, 1977). The higher ambient lead levels were associated with a primary lead smelting operation located in the region.

The particle size distribution of lead aerosols are dependent upon the emission source. Urban aerosols collected in several cities whose air pollution problems stem mainly from vehicular traffic contain lead particles with a mass median equivalent diameter of 0.25 μ (Robinson and Ludwig, 1967). Over 90 percent of the lead-containing particles are less than 1 μ in diameter (Jenkins, 1976). The particle-size distribution of atmospheric lead particles collected near a primary lead smelter is somewhat different (as seen in Figure 2-3). A larger portion of the lead-containing particles are in the $\geq$ 7.0 μ size region. These larger particles are not as likely to penetrate into the pulmonary regions of lungs. Rather, they are deposited in the nasopharyngeal region, removed via the mucociliary escalator, and either swallowed or expectorated. It

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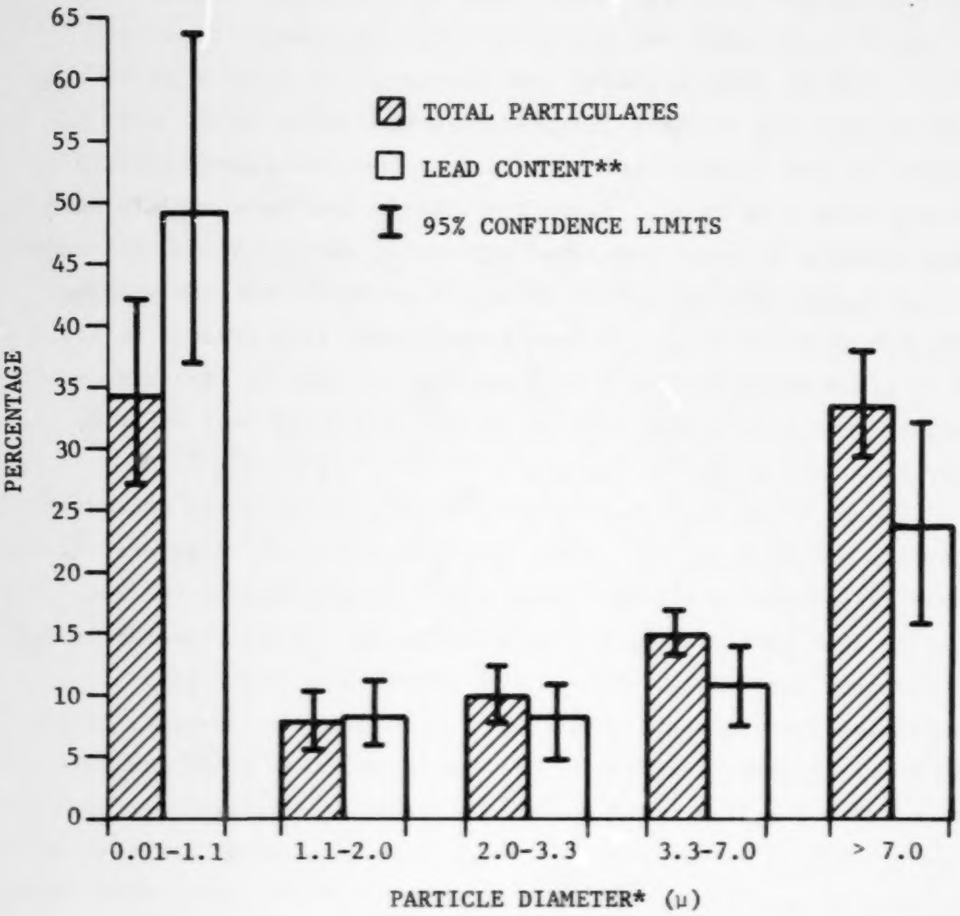
*AQCRs were required under the 1967 amendments to the Clean Air Act of 1963, and based on "jurisdictional boundaries, urban-industrial concentrations and other factors necessary to provide adequate implementation of air quality standards" (EPA, 1972b).



*Mean: August 1972-July 1973; one set of samples each month

**Mean: January-July 1973; one set of samples each month

SOURCE: Landrigan et al., 1975

FIGURE 2-3
SIZE DISTRIBUTION AND LEAD CONTENT OF AIRBORNE SUSPENDED PARTICULATES, EL PASO, TEXAS (ALL SAMPLES COLLECTED IN SMELTERTOWN, 250 METERS FROM THE SMELTER STACK)

has been estimated that approximately 75 percent of the lead-containing particulate material of an atmosphere, such as illustrated in Figure 2-3, would be nonrespirable (EPA, 1972a). Larger particles are also more apt to settle out of the atmosphere quickly. Therefore, they contribute significantly to the lead levels in dust, soil, water, and vegetation in the vicinity of the source.

In areas close to main transportation arteries, atmospheric lead concentrations can vary substantially. The level of atmospheric lead near a roadway has been shown to vary directly with the volume of vehicular traffic and the size of the community traversed (Hall, 1972; Johnson et al., 1978; NAS, 1972). Mean atmospheric lead levels in the Los Angeles area have been shown to vary from 9.4 to 38.0 $\mu g/m^3$ according to proximity to freeways, time of day, day of the week, and sampling elevation* (NAS, 1972). Such sampling regimes may include both respirable lead particles and coarser, nonrespirable lead particles, since many of the larger particles would not necessarily have settled out of the atmosphere prior to sample collection. Empirical measurements in the immediate vicinity of freeways in Los Angeles have indicated that from 20 to 40 percent of the lead particles collected were larger than 2.14 μ in diameter (Atkins and Krueger, 1968).

NASN quarterly composite samples of airborne lead concentrations for a given state or metropolitan area represent average lead concentrations recorded by a hi-vol sampling network. The sampling sites, usually stationed on rooftops, do not accurately depict the situation at street level. Heavily trafficked urban areas yield high low-level air-lead concentrations due to vehicular exhaust (Goldgraben, 1978).

More than 50 percent of street level vehicular particulate air lead is deposited on nearby surfaces before transmission to higher altitudes can occur (this percentage is representative of highway speeds; slower city traffic would be expected to raise the percentage of early lead deposition) (NAS, 1972; Huntzicker et al., 1975). Vertical gradient studies only exist for short-term analysis of lead concentrations. Reliable analysis should be based on long-term simultaneous measurement at low and high altitudes. Short-term low level urban vertical air analyses depict average lead concentrations of 8 $\mu g/m^3$, while NASN annual averages indicate much lower air-lead values ($<1\ \mu g/m^3$) (Darrow and Schroeder, 1974; Edwards, 1975; EPA, 1977). The extent of this underestimation is not easily quantified, due to action of confounding microclimatic factors (e.g., street canyon effects, eddying, vehicle speed, and crosswind effects) (EPA, 1977).

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*Sampling times ranged from 2 to 9 hours, but this variation did not appear largely responsible for the differences in reported levels.

Horizontal dispersion studies of vehicular particulate lead near traffic arteries (vehicles at highway speeds) indicate deposition of greater than 50 percent of emitted lead within 150 feet of a highway, with concentrations decreasing with increasing distance (Daines et al., 1970; Lagerwerff and Specht, 1970; NAS, 1972). Horizontal displacement of NASN sampling sites away from busy intersections would, again, underestimate particulate air lead concentrations characteristic of exposure adjacent to street level sources in the urban environment.

Other factors impacting those individuals exposed to street level vehicular lead particles include the resuspension of particulate lead deposited on and near the road surface, and the effect of airborne street level lead containment within the indoor environment. Again, NASN samplers would be insensitive to these factors due to rooftop locations. The resuspension of settled vehicular lead on roadways by passing vehicles increases as a function of vehicle speed (Sehmel, 1976). Resuspension of 1 to 5 percent of lead deposited on roads by passing vehicles has been estimated (Sehmel, 1976). Air-lead levels in houses adjacent to heavily traveled roads are almost identical with outside street air-lead levels, and fluctuate with the same diurnal cycles (Butler and MacMurdo, 1974).

2.2 Lead Concentrations in the Diet

Although the ingestion of food containing lead appears, on the average, to be a large contributor to an adult's total daily lead intake, the exact quantity is a function of the type and size of the diet. The occurrence of lead in various foodstuffs may be a result of natural bioaccumulation, deposition of airborne lead particles, and/or food processing and serving.

Since most foods have been found to contain about 0.5 ppm of lead or less, intake depends more upon the size and nature of the diet than on a choice of particular foods (Schroeder and Balassa, 1961). However, some segments of the population with special dietary requirements, such as infants, may consume selected foods found high in lead content (e.g., canned milk). As a result, they ingest more lead than might be expected based on average adult dietary constituents. The lead content of major food classes is presented in Table 2-3.

To distinguish degrees of health risk associated with particular dietary habits, estimates of total dietary lead exposure have to reflect frequency distribution data on lead levels in specific food commodities in relation to the quantities actually ingested by various sample populations. Several studies have estimated total daily ingested lead for several typical adult populations based on total food consumption, food class preference, and lead levels in the foodstuffs (see Table 2-4). Each estimate of daily lead intake is based on various assumptions, as specified in the appropriate column of the table. In some instances two estimates of total dietary lead intake are provided; one including the lead contribution from beverages (FDA food category XII), in addition to all other food categories, and one excluding beverages. The revised estimate of daily lead intake (i.e., excluding beverages) is provided, so that later calculations considering lead contributions from both food and drinking water will not result in double-counting. Since normal beverage consumption

TABLE 2-3

LEAD CONTENT IN SELECTED FOODS

	FOOD CLASS*	LEAD CONTENT (ppm)	REFERENCE
I	Dairy Products		
	Raw cow's milk	0.02	FDA, 1975
	" " "	0.091	Bruhn and Franke, 1976
	" " "	0.05	Lamm and Rosen, 1974
	" " "	0.04	Mitchell and Aldous, 1974
	Human breast milk	0.012	Murthy and Rhea, 1971
	" " "	0.05	Lamm and Rosen, 1974
	" " "	0.026	Dillon et al., 1974
	Evaporated milk, canned	0.02	Mitchell and Aldous, 1974
	" " "	0.11	Lamm and Rosen, 1974
	" " "	0.81	Murthy and Rhea, 1971
	" " "	0.05	Schroeder and Balassa, 1961
	Infant formula	0.08	Lamm and Rosen, 1974
	" "	0.42	Murthy and Rhea, 1971
II	Meat, Fish and Poultry		
		0.015	FDA, 1975; Kolbye et al., 1974
	Cured meats	0.06	Kirkpatrick and Coffin, 1973
		0.21	Schroeder and Balassa, 1961
		0.013	Mahaffey et al., 1975
III	Grain and Cereal Products		
		0.012	FDA, 1975; Kolbye et al., 1974
		0.37 (wet)	Schroeder and Balassa, 1961
		0.20 (dry)	Garcia et al., 1974
		0.10	Mahaffey et al., 1975
IV	Potatoes		
		0.004	FDA, 1975; Kolbye et al., 1974
		0.12	Schroeder and Balassa, 1961
		0.04	Thomas et al., 1972
		0.003	Mahaffey et al., 1975
V	Leaf vegetables		
		0.054	FDA, 1975; Kolbye et al., 1974
		0.05	Mahaffey et al., 1975
		0.3	Schroeder and Balassa, 1961
		0.08	Thomas et al., 1972

TABLE 2-3 (CONCLUDED)

	FOOD CLASS*	LEAD CONTENT (ppm)	REFERENCE
VI	Legume vegetables		
		0.265	FDA, 1975; Kolbye et al., 1974
		0.02	Schroeder and Balassa, 1961
		0.26	Mahaffey et al., 1975
VII	Root vegetables		
		0.11	Mahaffey et al., 1975
		0.131	FDA, 1975; Kolbye et al., 1974
		0.04	Thomas et al., 1972
VIII	Garden fruits		
		0.11	FDA, 1975; Kolbye et al., 1974
		0.12	Mahaffey et al., 1975
		0.02	Schroeder and Balassa, 1961
		0.06	Thomas et al., 1972
		0.06	Thomas et al., 1973
	Canned	0.85	Thomas et al., 1975
IX	Fruits		
		0.031	FDA, 1975; Kolbye et al., 1974
		0.043	Mahaffey et al., 1975
		0.04	Schroeder and Balassa, 1961
		0.1	Thomas et al., 1973
	Canned	0.56	Thomas et al., 1973
X	Oils, Fats, and Shortening		
		0.013	Mahaffey et al., 1975
		0.015	FDA 1975; Kolbye et al., 1974
XI	Sugar and Adjuncts		
		0.007	Mahaffey et al., 1975
		0.008	FDA, 1975; Kolbye et al., 1974
		0.07	Schroeder and Balassa, 1961
XII	Beverages		
	All Beverages	0.004	Kolbye et al., 1974
		0.003	Mahaffey et al., 1975
	Beer	0.01	Hardy, 1965
		0.01-0.29	de Treville, 1964
	Wine	0.08-0.86	Hardy, 1965
		0.05-1.5	de Treville, 1964

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[*] Food group category according to FDA, 1975

TABLE 2-4

ESTIMATED DAILY LEAD INTAKE FROM FOOD: ADULTS

Estimated daily Pb intake, Adults (μg/day) Including beverages	Estimated daily Pb intake, Adults (μg/day) Excluding beverages	Reference	Remarks
57	55	Kolbye et al., 1974	Based on average daily diet of 18-year old male consuming 2922 g/day of food (2225 g/day excluding beverages); estimate based on FDA FY1973 Total Diet Study, where analytical results for Pb reported "trace amounts" and "nondetections" = 0).
66		Morse and Welford, 1971	Based on normal diets of New York City residents, estimated from USDA consumption figures.
73-86		Bogen et al., 1976	Based on estimated daily intake of 19 food product categories.
90		FDA, 1977	Same as Kolbye et al. (1974), above; estimate based on FDA FY1974 data.
95		FDA, 1977	Same as above; estimate based on FDA FY1974 data; analytical results for Pb assumed "trace amounts" = 0.02 ppm (half of lowest quantitated level), and "nondetections" = 0).
100 113	90 102	Griffin et al., 1975	Based on actual diets of two prisoner populations, for up to a 4-month duration; average total daily food intake was 1929 g; daily Pb intake from beverages assumed to be 10% (see Kolbye et al., 1974).
120-350		Kehoe, 1964	Based on mean quantity of lead ingested by 10 healthy adults (food and beverages) over periods of time extending beyond 2 years.
141		FDA, 1977	Based on average daily diet of 18-year old male consuming 2922 g/day of food; estimate based on FDA FY1974 Heavy Metals in Food Survey, using median levels of surveyed foods.

TABLE 2-4 (CONCLUDED)

Estimated daily Pb intake, Adults (µg/day)		Reference	Remarks
Including beverages	Excluding beverages		
159	144	Kolbye et al., 1974	Based on average daily diet of 18 year old male consuming 2922 g/day of food (2225 g/day excluding beverages); estimate based on FDA FY1973 Total Diet Study, where analytical results for Pb assumed "traces" = 0.09 ppm, and "nondetections" = 0).
170		Goldberg, 1975	Assumed average daily intake.
200		Tolan and Elton, 1972	Average daily intake (United Kingdom); no specific food category provided major source of lead.
233	191	Kolbye et al., 1974	Same as Kolbye et al. (1974) above; except analytical results assume "traces" = 0.09 ppm and "nondetection" = 0.05 ppm.
254	208	FDA, 1975	Same as above; except estimate based on FDA FY1974 Heavy Metals in Food Survey, using mean levels of Pb in surveyed food; daily intake excluding beverages based on percent contribution of that food class in FY1973 data.
258		Schroeder and Balassa, 1961	Based on institutional diet for one day of 2526 g, including beverages.
274		Thompson, 1971	Based on actual diet of five individuals determined over a number of consecutive days (12-28 days).
300		Stoewsand, 1972	Estimated average daily intake.

appears to provide less lead uptake than equivalent amounts of water (see Table 2-3), it would be conservative to assume that all beverage lead intake was in the form of drinking water.

Table 2-5 provides similar estimates for daily lead intake by children ranging in age from 6 months to several years. As noted in the appropriate columns, infants' diets varied from special formula to normal adult foods. In most instances, the drinking water category is only included in the data for children 2 years and older.

2.3 Lead in Drinking Water

Lead is a natural, although often minor, constituent of surface and ground waters. The amount of lead dissolved in water depends upon the equilibrium constants of the chemical form(s) of lead present. These equilibrium constants depend, to some extent, upon the chemical characteristics of the water system. Studies of lead equilibrium solubilities of a variety of inorganic lead compounds show that water could contain from several micrograms to several hundred micrograms of lead per liter of water, depending upon the pH, temperature, and mineral content of the water (Durum, 1974; Hem and Durum, 1973). Empirical evidence indicates that surface and ground water used in domestic water supplies contains inorganic lead in concentrations averaging less than 10 μg/l (Kopp and Kroner, 1967).

In a survey encompassing over 700 surface water sites in the United States and Puerto Rico, less than 0.5 percent of the samples exceeded 50 μg lead per liter of water (Hem and Durum, 1973). A larger proportion of the waters in the northeastern and southeastern states contained lead above the detection limit (1 μg/l), and the northeastern and southeastern states had the largest share of those samples reporting lead > 10 μg/l.

Lead present in drinking water above that concentration found in the make-up water usually occurs as a result of the physical characteristics of the water distribution system. The use of lead pipes

TABLE 2-5

ESTIMATED DAILY LEAD INTAKE FROM FOOD: CHILDREN*

Age	Estimated daily Pb intake (μg/day)	Reference	Remarks
Infant (breast fed)	40	Alexander et al., 1972	
1 mo.	90	Alexander et al., 1972	**Hospital patients with inborn errors of metabolism fed a synthetic diet.**
2 mo.	79	FDA, 1975	Based on FY1974 Total Diet Study (FDA).
6 mo.	63	" "	" " " " " " "
1 yr.	100	" "	" " " " " " "
2 yr.	115	" "	**Based on FY1974 Total Diet Study (FDA)**, based on average daily intake of 1555 **g.**
6 mo.	100	Kolbye et al., 1974	Based on average daily intake of 1363 **g, consisting of "adult table** foods"; analytical results for Pb reported "traces" = 0.09 ppm, **"nondetections" = 0.**
6 mo.	119	Kolbye et al., 1974	Based on average daily intake of 1363 **g, consisting of infant foods.**
6 mo.	71-77	FDA, 1975	Based on FY1973 Total Diet Study and National Canner's Association figures.
1-12 mo.	93	Kolbye et al., 1974	Estimated average daily intake.
1-3 yr.	130	Barltrop and Killala, 1967	Estimated average daily intake.
2 yrs.	73-75	Kolbye et al., 1974	Based on average daily intake of 1561 **g, consisting of "adult** table foods."
20-30 mo.	110	FDA, 1975	Based on actual diet of 12 children on two separate days.
4 yrs.	135	FDA, 1975	Based on FDA Total Diet Study and National Canner's Association figures.
6 yrs.	154	FDA, 1975	" " " " " " " " " " "
8.5 yrs.	240	Alexander et al., 1972	Hospital patients with inborn errors of metabolism.

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*Drinking water is included in the diet of the 2-year and older children; the <2 year infant's fluid intake assumed from foodstuffs.

within the system (e.g., service line from water main to individual homes, home plumbing systems) provides an opportunity for the lead in contact with the water to go into solution. The degree of plumbosolvency of the water is a function of temperature, pH, and hardness (Moore, 1975; Waldron and Stofen, 1974). In general, acidic, soft-water areas are particularly prone to high lead concentrations. In such areas, the acidity of the water increases its ability to dissolve the metal from lead pipes, and the low concentration of calcium impairs the formation of a calcium carbonate layer which, in hard-water districts, lines the pipes and impedes solution of the lead (Waldron and Stofen, 1974).

Studies have indicated that the lead concentration in tap water from a house using lead pipe in the plumbing system is a function of the total length of lead piping that the water traverses (Schroeder and Balassa, 1961; Waldron and Stofen, 1974; Moore, 1975, 1977). In addition, the use of lead-containing soldering alloys to join copper pipes, the use of lead storage tanks, and the grounding of electric wires to lead pipes (solution via electrolysis) increase the lead content in drinking water (Waldron and Stofen, 1974; Wong and Berrang, 1976; Goldberg, 1974). The lead content in tap water from homes with lead pipes in the plumbing system depends upon the length of time the water sits in the pipes. Lead concentrations are much higher in water that has remained in the pipes overnight than in samples taken after the system has been thoroughly flushed (Schroeder and Balassa, 1961; Wong and Berrang, 1976).

2.3.1 Lead in Potable Water Distribution Systems

In a study by McCabe et al. (1970), lead concentrations in finished drinking water collected at 969 public water supply systems in the United States ranged from an undetectable amount to 640 μg/l. Of the supply systems sampled, 37 sites (1.4 percent of the total) contained lead in concentrations exceeding the current national interim primary drinking water standard of 50 μg/l (McCabe et al., 1970). In a similar survey that examined the water supplies of the 100 largest U.S. cities, Durfor and Becker (1964) found that 95 percent contained lead at concentrations less than 10 μg/l, with a median value of 3.7 μg/l. The maximum reported lead concentration in that study was 61 μg/l. In a more recent survey of 592 interstate carrier water supplies (EPA, 1975), only two sites (0.3 percent of the total) reported lead levels in excess of 50 μg/l. In a reconnaissance survey of 253 public water supplies, 79 sites did not detect lead concentrations greater than 1 μg/l. Of those 174 sites reporting measurable quantities of lead, the average was 6.2 μg/l, with a maximum of 34 μg/l (Durham et al., 1971).

Additional surveys of individual U.S. water supplies have indicated the presence of lead in potable water supplies at concentrations exceeding 50 μg/l. In the nine-area* Community Water Supply Study (Bureau of Water Hygiene, 1970 a-d), several sites reported lead concentrations in excess of 50 μg/l, with a maximum value of 497 μg/l occurring in one New York City suburban area.

Studies at particular sites have indicated lead concentrations that exceeded the current interim standard in some water systems. In Colorado, for example, lead samples averaged 45 μg/l in the systems surveyed, with a maximum reported level of 100 μg/l (Roberts et al., 1975). In eastern South Carolina (Georgetown County), 3 percent of the water supplies contained lead levels exceeding 50 μg/l (Sandhu et al., 1975). Since these were not intended to be comprehensive surveys of potable water supplies in the particular geographical area, their frequency-of-occurrence data are not necessarily representative of that area of the country. Lead levels in water supply systems are presented in Table 2-6.

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*Those sites included in the following Standard Statistical Metropolitan Areas (SMSAs): San Bernardino-Riverside-Ontario, California; Vermont; Kansas City, Missouri; Cincinnati, Ohio; New Orleans, Louisiana; Charleston, West Virginia; Charleston, South Carolina; Pueblo, Colorado; and New York, New York.

2.3.2 Lead in Tap Water

Tap water tends to contain higher lead concentrations than water in distribution systems due to the use of lead pipe or lead-containing solder in the plumbing systems. Table 2-7 provides lead levels in tap water collected from homes possessing a range of plumbing systems. The lead levels vary from several hundred to several thousand micrograms of lead per liter of water.

It is very difficult to estimate the average lead levels in households across the country, because of variations in the chemical properties of local water and home plumbing systems. However, several studies have attempted to gauge lead levels locally by collecting water from representative homes within a community water supply district (see Table 2-8). The variation in lead concentrations over time for a particular location can be partially explained by changes in treatment technique.

2.4 Additional Sources of Childhood Lead Exposure

Lead-containing nonfood substances are deliberately or inadvertently ingested by some individuals. This is especially prevalent and frequent in young children (Lourie et al., 1963; Day et al., 1975; Lepow et al., 1974), many of whom display patterns of repetitive hand-to-mouth activity, mouthing behavior, or pica. Hand-to-mouth activity coupled with the presence of foreign substances (particularly soil and dust) on the hands and ingestion of soil- and dust-contaminated food may both result in the ingestion of appreciable quantities of lead. Mouthing of substances containing or contaminated with lead, or pica for such substances, may also be

TABLE 2-6

LEAD CONCENTRATIONS IN DRINKING WATER SUPPLIES EXCEEDING NATIONAL INTERIM PRIMARY STANDARD (50 μg/1)

Lead Concentration (μg/1)	Location	Reference	Remarks
62 (max)	Public water systems	Durfor and Becker, 1964	In analyzing public water supplies of the 100 largest U.S. cities, 95% contained less than 10 μg/1, with median of 3.7 μg/1.
70 (avg)	Pueblo County, CO; public water supply	Bureau of Water Hygiene, 1970a	From Community Water Supply Study; average Pb concentration in one water system.
81 (avg)	Kansas City area; public water supply	Bureau of Water Hygiene, 1970b	Platte County water district; maximum reported level, 152 μg/1.
100 (max)	Community water supply (Colorado)	Roberts et al., 1975	Colorado State Department of Health data, 1970; remaining samples averaged 45 μg/1.
118 (max)	Riverside, CA; public water supply	Bureau of Water Hygiene, 1970c	Intercity mutual water supply; average concentration reported, 39 μg/1.
132 (max)	Community water supply (North Carolina)	Sandhu et al., 1975	In waters surveyed, 3 percent exceeded 50 μg/1 level.
220 (max)	Interstate carrier water supply system	EPA, 1975	Of 592 supplies sampled, only New Bedford and Quincy, MA reported levels >50 μg/1 (less than 0.3% of total).
320 (max) 497 (max)	Distribution system Finished drinking water	Bureau of Water Hygiene, 1970d	From Community Water Supply Study, NY-SMSA; frequency of occurrence unknown.

TABLE 2-7

LEAD CONCENTRATIONS IN HOUSEHOLD TAP WATER EXCEEDING NATIONAL INTERIM PRIMARY STANDARD (50 μg/1)

Lead Concentration* (μg/1)	Reference	Remarks
160 (max)	Strain et al., 1975	Maximum value reported in water collected in 50 homes in the Northeastern
112	Schroeder and Balassa, 1961	Water obtained from spring, piped through 50 ft of lead pipe (~50 yrs old).
260	Wong and Berrang, 1976	Water collected in morning; system contained lead service line.
290 (max)	Roberts et al., 1975	12 samples collected in Nassau County, New York from homes with lead service lines; mean = 95 μg/1.
2500	Wong and Berrang, 1976	Water collected from tap not used in 6 months.
5500	Tolley, 1973	Total lead content of running drinking water delivered through lead pipes.
934	Goldberg, 1974	Water system had lead-lined holding tank, and lead piping.
239	Goldberg, 1974	Water system had no lead-lined holding tank, and >60 ft lead piping.
108	Goldberg, 1974	Water system had no lead-lined holding tank, and <60 ft lead piping.

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*Average levels unless otherwise indicated

TABLE 2-8

LEAD IN TAP WATER SAMPLES FROM HOUSEHOLDS IN SELECTED AREAS OF THE UNITED STATES

Location	Maximum Reported Value (μg/l)[d]	Average Reported Value (μg/l)	Percent of Samples Reporting Lead Levels Greater Than:			Sample Collection Date
			10 μg/l	25 μg/l	50 μg/l	
Bennington, VT[a]	475	163	100	100	100	4/77
	860	254	100	100	97	5/77
	125	36	77	40	27	6/77
	260	88	97	83	53	7/77
Fall River, MA[a]	620	155	90	87	63	6/76
	250	43	36	24	14	5/77
New Bedford, MA[a]	260	60	67	63	47	----
Cambridge, MA[a]	21	---	7	3	0	11/75
	40	---	30	15	0	6/76
Boston, MA[b]	680	68	---	---	33	5/76
	650	78	---	---	46	11/76
	350	45	---	---	32	7/77
Chicago, IL[c]	55	---	7.3	1.9	0.7	76-77

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[a] 10 houses sampled, 3 samples per house (standing and flushed systems)

[b] 18-22 houses sampled, 3 samples per house (standing and flushed systems)

[c] 1293 households sampled

[d] Maximum reported value in limited survey; not necessarily representative of current systems

SOURCE: Adapted from Lassovszky, 1978.

a mechanism of lead exposure. The list of substances commonly mouthed or ingested by children displaying these behaviors has been shown to include paper (newspaper, wallpaper, toilet tissue, facial tissue, cardboard), dirt (soil, dust, clay, sand, ashes), paint and plaster, tobacco, and toiletries and cosmetics (Barltrop, 1966; Millican et al., 1962). Some of these are known to contain lead. Concentrations of lead that have been measured in these substances are reported in the following sections.

2.4.1 Soil/Dust*

Anthropogenic sources are responsible for the major portion of lead found in soil and dust. Natural occurrence of lead in the earth's crust accounts for an average of 15 μg/g (Durum et al., 1971). Mean rural soil and dust lead levels of 60 and 275 μg/g have been reported (Rolfe and Haney, 1975; Bethea and Bethea, 1975). However, lead levels in soil and dust in metropolitan areas are said to be as high as 20,000 μg/g (Jenkins, 1976). The mean interior house dust-lead level for an urban area was reported as 11,000 μg/g (Lepow et al., 1974). Metropolitan soil-lead levels as high as 3357 μg/g have been reported (NAS, 1972).

The combustion of leaded gasoline is a major contributor to the high lead levels in urban soil and dust (NAS, 1972). Lead levels of about 75 to 730 μg/g have been found in soil adjacent to low and high traffic volume streets, respectively (Johnson et al., 1978). Additional data from this study suggest a correlation between urban air-lead concentrations and lead levels in hand-wipe samples from children. Since urban atmospheric lead concentrations are related to traffic volume (Section 2.1), these indicate a relationship between gasoline combustion and urban soil/dust-lead. Soil lead concentrations diminish with distance from roadways, but increase significantly near dwellings (Rolfe and Haney, 1975). Increased levels of soil lead near dwellings have been reportedly due to runoff of lead particulates from vehicular aerosol deposition (Rolfe and Haney, 1975), and from the weathering of paint on outer surfaces of dwellings (Ter Haar and Aronow, 1974). High interior dust lead levels (11,000 μg/g) on unpainted surfaces were reported to be a result of outdoor vehicular aerosol contamination (Lepow et al., 1974). Soil concentrations near U.S. highways displayed decreased concentrations with increased distance from roadways, as well as with increased soil depth. Lead concentration reduction of 65 to 75 percent occurred within a distance of 24 meters from the road (from 32 to 8 μg/g) where traffic densities ranged from 7500 to 48,000 cars per day (Lagerwerff and Specht, 1970).

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*Soil and dust will be treated as a single entity in later calculations and therefore will commonly be designatd "soil/dust".

Industrial point sources (e.g., smelters and battery plants) are a major local source of soil/dust-lead contamination. Air and soil levels were shown to decrease with increased distance from a smelter site in El Paso, Texas. Soil lead concentrations within 1 mile of the smelter averaged 36,853 μg/g, but declined to 2726 μg/g at 1.1 to 2.0 miles and to 2151 μg/g at distances over 4 miles (Landrigan et al., 1975). A smelter study in Silver Valley, Idaho, displayed significantly increased air and soil-lead levels at distances of up to 16 miles from the source (Idaho Department of Health and Welfare, 1977). It is apparent that industrial point sources of lead emissions can affect soil levels for much greater distances than those induced by low level vehicle emissions.

Lead particles are emitted from vehicles initially as halogenated compounds, of which lead chlorobromide is the most abundant. These lead particulates lose the halogens, shift toward small particle sizes, and increase their water solubility during airborne transport via chemical reactions which are enhanced by light and SO_2. Lead oxide, lead carbonate, and lead sulfate are the major chemical forms prevalent after deposition of lead particles (Ter Haar and Bayard, 1971; EPA, 1977). These results are in agreement with Olson and Skogerboe (1975), who found the major lead contaminant of soil and dust to be lead sulfate.

2.4.2 Paint

Ingestion of paint by children suffering from pica has been associated with numerous cases of childhood lead poisoning. Epidemiological evidence indicates an association between elevated blood-lead levels and children with pica for paint (NAS, 1972).

Pica for paint is of major concern. Extremely high lead concentrations are found in some older paint coatings and are still available as peeling and flaking paint (indoor and outdoor) on older dwellings. A survey of over 2000 dwellings in Pittsburgh revealed that at least 20 percent of the residences built after 1960 had at least one surface with an excess of 1.5 $\mu g/cm^2$ lead (Shier and Hall, 1977). Smaller surveys in El Paso, Texas and Silver Valley, Idaho, found indoor paint-lead concentrations of >1 percent by weight (10,000 $\mu g/g$) (Landrigan et al., 1975; Idaho Department of Health and Welfare, 1977).

Market surveys in 1971 showed 8 of 76 paints tested contained 2.6 to 10.8 percent lead. The Consumer Product Safety Commission found that only 2 percent of interior paints tested had lead levels exceeding 1 percent (NAS, 1976). The same survey found that 70.8 percent of oil-based paints and 96.1 percent of water-based paints contained less than 0.06 percent lead (the current paint standard).

Regulation of the use of lead in house paints did not exist until 1955, when a 1 percent voluntary standard was adopted. A federal standard of 1 percent was imposed in the early 1970s, lowered to 0.5 percent in 1976, and further lowered to 0.06 percent (600 $\mu g/g$) in 1977. It is apparent that paint with lead levels in excess of 1 percent (by weight) is still readily accessible to children who live in older dwellings (NAS, 1976).

2.4.3 Newsprint

Newsprint can be comprised of up to 1 percent lead (by weight) (Hankin et al., 1974). Colored newsprint contains the greatest amounts of lead. Handling newsprint may result in appreciable dermal exposure; and, coupled with immature dietary habits (e.g., the licking and sucking of fingers), newsprint may represent a source of ingested lead as well. Ingestion of newspaper is common among children with pica. Indirect newsprint-related exposure can result from elevated air lead levels in homes where newspapers and magazines are used as fireplace fuel (Perkins and Oski, 1976).

2.5 Other Lead Sources

2.5.1 Lead-Glazed Utensils

A number of persons have been poisoned by lead that has leached from glazed kitchen utensils. Studies have indicated that the amount of lead leaching into a beverage from the glaze of a ceramic vessel is a function of the temperature at which the glaze was fired, how long the drink has remained in the vessel, the pH of the drink, and the number of times the vessel had been used previously. In one study, lead concentrations in a cola (pH 2.7) stored in a glazed mug increased by 2800 μg/l after two minutes and by 6600 μg/l after two hours of containment (Harris and Elsea, 1967).

2.5.2 Occupational Exposures

Workers whose occupations entail chronic exposure to high lead levels (e.g., garage mechanics, police, smelter workers) have been shown to have higher mean blood-lead levels than other workers (EPA, 1972a; Johnson et al., 1975b). In some studies, more than 50 percent of such high risk populations have been shown to have blood-lead levels ≥ 40 μg/dl, far higher than the 1 to 5 percent representative of the average adult population (EPA, 1972a).

Prudent industrial hygiene practices can minimize excessive occupational lead exposure. Since this discussion is centered around the possible environmental lead exposure sources, as opposed to specific occupational categories, occupational lead exposures will not be discussed further.

2.5.3 Smoking

Tobacco smoke is an additional source of respiratory lead exposure. Reports indicate that inhaled cigarette smoke may provide from 20 to 66 μg of lead per pack (Schroeder and Balassa, 1961; Patterson, 1965). Contrasting information suggests that the high blood-lead levels in some individuals who smoke can be attributed to the contamination of fingers and cigarettes from nontobacco sources and the deleterious effects of smoking upon lung clearance mechanisms (Tola and Nordman, 1977).

3.0 ABSORPTION, RETENTION AND ELIMINATION OF LEAD IN HUMANS

Lead is absorbed into the body via inhalation, ingestion, or dermal contact, enters the bloodstream, and is transported throughout the body. The concentration of lead in the body is a function of the level and duration of exposure, the rate of absorption, and the rate of elimination.

Once lead has entered the bloodstream, it can be transported to most sites within the body. Lead is removed from the blood by excretory mechanisms (e.g., kidney) or by gradual accumulation at various storage sites (e.g., soft tissue, bone). Toxic symptoms result when the lead concentration in a particular body compartment is sufficient to cause damage. When assessing the toxicological implications of environmental lead exposure, it is important to consider the exposure route because the kinetics of absorption vary between routes.

3.1 Absorption Characteristics

Environmental lead compounds can be absorbed into the bloodstream from the lung after inhalation, from the gastrointestinal tract after ingestion, or to a limited extent, from direct dermal contact. The absorption kinetics for each of these pathways are dependent upon a number of factors, including the physical and chemical nature of the lead compounds at the time of exposure and the presence of other modifying agents. Once inorganic lead is absorbed into the bloodstream (where it is mainly bound to erythrocytes [Butt et al., 1964]), it is readily transported to other locations in the body and does not normally retain any characteristics associated with its exposure or absorption route. Although inhalation and ingestion of lead-containing compounds are the predominant routes of intake, dermal absorption may be significant under certain circumstances (e.g., occupational lead alkyl exposure). The three absorption routes are discussed in detail in the following sections.

3.1.1 Pulmonary Absorption

To be absorbed into the bloodstream, inhaled lead material must be retained in the lower regions of the lung (pulmonary region) long enough to be solubilized. Lead vapors freely penetrate deeply into the lung, but the penetrability of lead-containing aerosols is dependent on several variables, the predominant one being particle size. Since most atmospheric lead compounds exist as a component of particulate matter, the uptake of lead vapors can be ignored (Smith, 1971).

Physical retention of particulate matter in the lung is a function of particle size and breathing kinetics, while the chemical properties of the particle determine its solubility in body fluids, and hence its ultimate absorption. If particles are deposited in the upper regions of the respiratory tract (i.e., nasopharyngeal and tracheobronchial regions), they can be removed by the ciliated epithelium (mucocilary escalator) relatively quickly and expectorated or swallowed. Particles deposited in the pulmonary (i.e., alveolar) region, which is devoid of cilia, can be absorbed into the bloodstream or phagocytized by alveolar macrophages and removed via the lymphatic system (Casarett and Doull, 1975). If a particle is larger than about 10 μ in diameter, it is deposited by inertial impaction in the nasopharyngeal region and removed. Particles between 1 and 5 μ often settle out in the tracheobronchial region and are similarly removed. Various lung deposition models suggest that the greatest retention in the pulmonary region of the lung occurs for particles with an aerodynamic diameter in the 0.1 to 1 μ range (Task Group on Lung Dynamics, 1966; Nozaki, 1966).

As indicated in Section 2.1, the particle size distribution of ambient lead aerosols tends to be within the respirable range.

However, one should not assume that all of the respirable lead material inhaled is subsequently absorbed into the bloodstream because the chemical form of the particle can affect the rate of absorption (Smith, 1971; Kehoe, 1969). The major species of atmospheric lead particles include various lead halide mixtures and lead oxide, phosphate, or sulfate (NAS, 1972). Since some of these compounds tend to be only slightly soluble in biological fluids, it is difficult to predict the degree to which they are actually absorbed within the lung.

Empirical evidence, from lead balance and lead tracer studies, indicates that from about 20 to 50 percent of inhaled lead particles (i.e., those particles representative of urban atmospheres) are absorbed into the bloodstream (see Table 3-1). In some cases, both retention in the lung and absorption into the bloodstream were monitored; while in other cases, only particle retention was determined with subsequent absorption assumed. Based on these studies, 40 percent is a reasonable value for lead absorption into the bloodstream from ambient lead aerosols in an adult.

The absorption of lead from ambient aerosols by children is not as well defined. Several problems, including differences in respiratory physiology, metabolism, and body compartment size, make absorption projections in children, based on data from adult, tenuous (Knelson, 1974). In addition, ambient monitoring data may not necessarily reflect the actual atmospheric dose to which a child (or an adult) is exposed, since there is often an increase in the particulate concentration gradient as one approaches ground level (see Section 2.1). Without definitive clinical studies of atmospheric lead retention and absorption in children, one must make projections based on adult data and modify them by known differences in ventilatory exchange. As a result, one must assume similar absorption and retention characteristics in adults and children but varying exposures.

TABLE 3-1

ABSORPTION CHARACTERISTICS OF INHALED LEAD COMPOUNDS IN HUMANS

Percent Absorbed	Reference	Remarks
20	Chamberlain **et al.**, 1975b	Initial lung deposition of lead particles in motor exhausts was 40 percent, 48 percent of which was absorbed into the blood.
29	Bogen **et al.**, 1976	Deduced from ^{210}Pb trace studies of urban populations inhaling ambient Pb aerosols.
29	Morse and Welford, 1971	As defined by ^{210}Pb dietary studies.
22-29	Chamberlain **et al.**, 1975a	Automotive exhaust particles; retention of particle in lung was 45 to 59 percent, while only 50 percent of that retained was absorbed into blood; data from radioisotope tracer studies.
25-30	Kehoe, 1964	Based on 30 percent particulate retention in lungs, 100 percent absorption of those particles retained; ambient urban atmospheric lead particles.
30-50	Schroeder and Tipton, 1968	Absorption of lead from normal urban atmospheres; 30 to 50 percent retention, of which 100 percent was absorbed.
34-60	Booker **et al.**, 1969	Determined with radiolead tracers; using particles 0.05 to 0.5 μm in diameter.
37-47*	Mehani, 1966	Retention of lead particles in an industrial setting (8-hr daily exposure period); retention not found to be dependent upon depth of breathing; no estimate of pulmonary lead absorption provided.
42.5-63*	Nozaki, 1966	Total pulmonary retention for particles 0.05 to 1 μm in diameter, respectively; tidal air volume 1350 cc.
50	Karhausen, 1972	Absorption of particles of less than 1 μm in diameter.
30-50	Kehoe, 1969	Retention of lead sesquioxide with mean particle size of 0.05 μm; virtually all lead particles deposited in lung assumed absorbed into blood.
40-50	Wetherill **et al.**, 1974	Absorption of total atmospheric lead.

*Percent retained

Inhaled lead-containing particles larger than one or two microns in diameter are usually collected in the nasopharyngeal or tracheobronchial regions of the respiratory tract, removed via ciliary action and expectorated or swallowed. That fraction which is swallowed may be absorbed in the gastrointestinal tract, but its contribution relative to other sources of ingested lead is unknown. Some studies utilizing artificially generated aerosols have indicated that up to 40 percent of inhaled lead particles (mass median diameter of 2.9 μ) deposited in the airways are transferred to the gastrointestinal tract (Kehoe, 1961). However, gastrointestinal absorption of inhaled lead from ambient urban atmospheres is expected to be insignificant given the particle-size distribution of such aerosols.

3.1.2 Gastrointestinal Absorption

The absorption of lead-containing compounds in the gastrointestinal (GI) tract is dependent upon the physical/chemical form of the material ingested, and can be affected by other factors including the composition of the diet and the age and physiological status of the individual. Absorption of lead from the GI tract appears to be a passive diffusion process, but may be regulated to some extent by the mechanisms controlling calcium and phosphorous absorption (Casarett and Doull, 1975; Gruden and Stantic, 1975).

In the average adult, approximately 10 percent of ingested lead is actually absorbed into the bloodstream. As indicated in Table 3-2, however, empirical evidence indicates large variations in the GI absorption of lead in humans. In some studies, the lead absorption in particular individuals approached 70 percent of the total amount ingested, but in most instances, a value of approximately 10 percent was reported. Such variations may be a result of individual GI tract differences, discrepancies between experimental protocols (e.g., balance versus tracer studies), chemical dissimilarities between the form of lead administered, or analytical error (Blake, 1976; Wetherill et al., 1974).

TABLE 3-2

ABSORPTION CHARACTERISTICS OF INGESTED LEAD COMPOUNDS IN HUMANS

	Percent Absorbed	Reference	Remarks
(Adult)	12.6	Thompson, 1971	Based on lead balance studies in 5 normal individuals; studies conducted for 12 to 28 days.
	8	Bogen et al., 1976	Based on ^{210}Pb tracer studies of urban population exposure; conforms to ICRP (1959) model predictions.
	8	Morse and Welford, 1971	Based on ^{210}Pb dietary studies.
	5-10	Kehoe, 1964	Determined from dietary balance studies.
	10-12	Kehoe, 1961	Empirically determined from clinical (dietary balance) studies of individuals consuming various lead salts.
	10	Goldberg, 1975	Based on amount ingested in normal diet, whether by food or water.
	10	Schroeder and Tipton, 1968	For food or water sources of dietary lead.
	6-45	Wetherill et al., 1974	Based on clinical studies for different diets, fasting, and chemical forms of lead.
	11.3	Blake, 1974	Isotopically labeled (^{203}Pb) study in 10 human volunteers; maximum retention in 1 subject was 67 percent.
	8-16	Chamberlain et al, 1975a	Based on radiotracer (^{203}Pb) studies in human volunteers ingesting motor exhaust particles.
	6-14	Rabinowitz et al., 1975	Absorption of lead from food based on lead tracer studies intestinal absorption ranged up to 70 percent during fasting.
(Child)	40	Mahaffey, 1977	Based on lead balance studies in 2-3 year olds.
	42	Ziegler et al., 1978	Based on balance studies in 10 infants and children aged 14 to 746 days.
	50	NAS, 1976	Representative average gastrointestinal absorption in infants.
	53	Alexander, 1974; Alexander et al., 1972	Balance study involving 8 healthy children, aged 3 mos to $8\frac{1}{2}$ yrs; retention of absorbed lead was 18 percent of intake.
	50	EPA, 1972b	Representative gastrointestinal absorption in children.

In children, the GI absorption of lead can vary, due in part to the source of the lead ingested and its physical/chemical characteristics. Based on data shown in Table 3-2, it is conservatively assumed that approximately 50 percent of the lead in food and water is absorbed. This fivefold difference in the GI absorption rates of children and adults has been related to the differences in the metabolic behavior of lead at different ages (Kostial et al., 1971; Momcilovic and Kostial, 1974). Experiments involving weanling rats fed lead chloride confirm the finding of substantially increased GI absorption in the young (Kostial et al., 1971; Forbes and Reina, 1972).

Children with pica may ingest a substantial amount of lead-containing substances. Paint is a source of lead for some children with pica. The lead in paint is believed to be absorbed at a different rate than lead in food and water. Animal studies have shown that lead in paint is not absorbed as well as the simple inorganic salts present in other sources. The data indicate that the forms of lead contained in paint are absorbed only one-fourth to one-half as well as the lead salts. A 17-percent rate of absorption for lead in paint has been estimated (NAS, 1976). It must be emphasized that due to high variability of several factors, this absorption rate is only suitable for use on a group basis.

No definitive studies have been conducted on the absorption rate for ingested lead from soil/dust. It appears that this is a major source of lead and that many children ingest substantial amounts of soil/dust from normal hand-to-mouth activity. It is generally assumed that within the gastrointestinal tract lead is more easily separated from the physically absorbed soil fraction than from the chemically bound fraction in paint. Analysis of lead in soil/ dust and paint from an area impacted by a smelter showed that 20 to 60 percent lead in surface soil was extractable in 0.1N HCl (representative of the human stomach) compared with less than 10 percent extracted from paint samples (Roberts et al., 1974). A rate of 30 percent has therefore been selected as a representative figure for the absorption of lead from soil/dust, reflecting an absorption rate intermediate between dietary lead and paint lead uptake.

A number of factors affect the degree of lead absorption in the GI tract. Variations in the chemical form of the ingested lead material can alter the absorption rate. Lead tracer studies in fasting adults have indicated that lead nitrate is absorbed at about three times the rate of lead sulfide (i.e., 41 and 14 percent, respectively) (Wetherill et al., 1974). Nutritional factors may also affect GI absorption of lead (Barltrop and Khoo, 1975a, b; 1976); short-term studies using ^{203}Pb tracer in rats detected a twentyfold increase in absorption for those animals fed diets deficient in minerals and a sevenfold increase for those on high-fat diets (Barltrop and Khoo, 1975a). There is also a pronounced tendency toward greater absorption when lead is ingested without food (Wetherill et al., 1974; Garber and Wei, 1974; Quarterman et al., 1976). Although it has been suggested that lead in drinking water is absorbed in the GI tract at twice the rate of lead in food (Patterson, 1965), definitive laboratory evidence of such a preferential absorption is currently unavailable. In the absence of such data, equivalent GI absorption rates for lead in food and water on the order of 10 percent in adults, and about 50 percent in children, have been assumed.

3.1.3 Dermal Absorption

In order to be absorbed through the skin, lead must either pass through the epidermal cell layer, the sweat or sebaceous glands, or the hair follicles. Uptake via the sweat glands or hair follicles is not significant. The epidermal layers are not highly permeable and restrict the absorption of most inorganic lead compounds. However, since the skin is a lipid barrier, organic lead compounds are able to pass through and be absorbed.

Clinical studies have indicated that organic lead compounds (e.g., lead naphthenate, lead acetate) can cross the epidermal layers to varying degrees and result in elevated blood-lead levels (Rastogi and Clausen, 1976). Alkyl lead compounds are also readily absorbed through the skin (Gething, 1975), and have caused episodes of acute lead poisoning.

The dermal absorption of lead compounds, however, does not appear to be a significant exposure route for the general population. Although organic lead compounds are quite capable of passing the skin barrier, the major source of exposure is occupational (e.g., garage mechanics, gasoline distributors). As mentioned in Section 2.1, alkyl lead concentrations in urban atmospheres are probably considerably less than 10 percent of the inorganic lead values (NAS, 1972).

3.2 Retention Characteristics

Postmortem analyses of tissue samples from persons with no occupational exposure to lead have demonstrated the presence of the metal in virtually every organ of the human body (Barry, 1975; Gross et al., 1975).

The body burden of lead is not distributed uniformly; lead has an extremely high affinity for calcareous tissue (Table 3-3). Over 90 percent of the lead stored in the adult body is located in the [illegible]eton. In one study (Barry, 1975), the average body burden of lead in 50 male adults was 164.8 mg, of which 155.5 mg (94.4 percent) was located in bone. Children were found to have both a substantially lower body burden of lead and a lower percentage of this body burden contained in their bones (Table 3-3). The average body burden of lead in 23 children (mean body weight 23 kg) was 12.3 mg, 72.5 percent of which (8.9 mg) was located in bone. However, concentrations of lead in the majority of soft tissues of children were either

TABLE 3-3

LEAD CONCENTRATIONS IN VARIOUS TISSUES OF CHILDREN AND MALE ADULTS
(ppm Wet Weight)

Tissue	Male Adults	Children (2-9 Years)
Tibia	23.4	3.70
Rib	8.85	3.01
Liver	1.03	0.87
Kidney		
Cortex	0.78	0.70
Medulla	0.50	0.49
Prostate	0.27	0.48
Spleen	0.23	0.13
Lung	0.22	0.19
Skin	0.19	0.63
Thyroid	0.19	0.28
Brain Cortex	0.10	0.09
Stomach	0.09	0.11
Heart	0.07	0.09

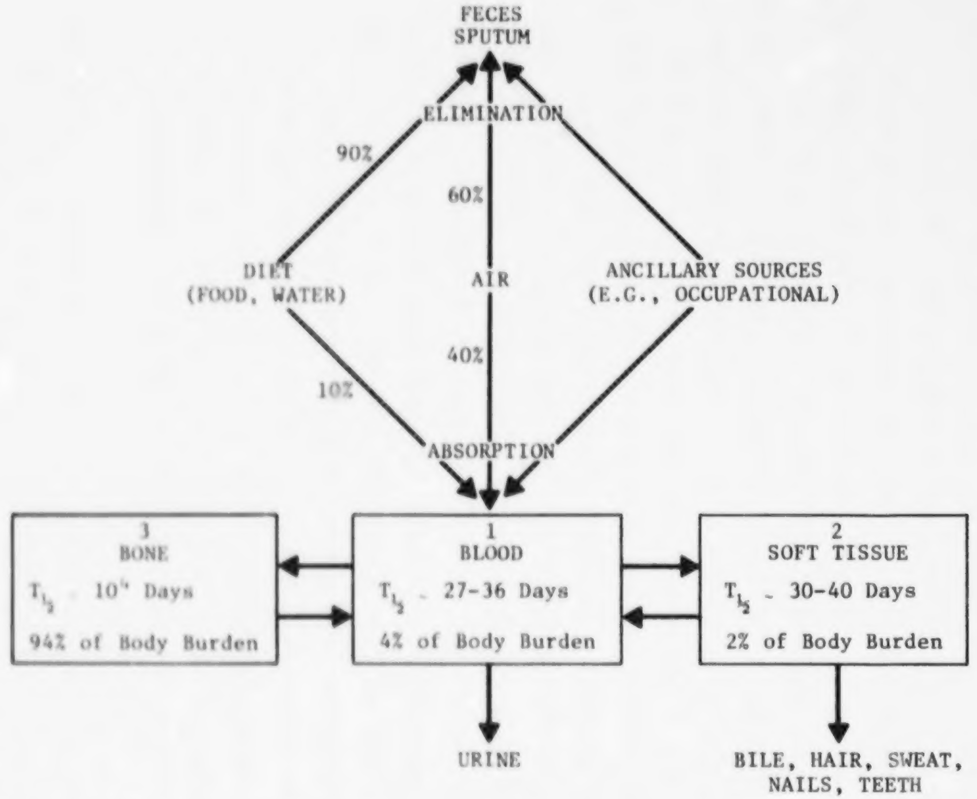
SOURCE: Adapted from Barry, 1975

the same as or higher than those in the corresponding tissues of adults (Table 3-3).

Lead concentrations in the majority of soft tissues apparently reach an equilibrium level during the second decade of life and remain at this level indefinitely (Barry, 1975). Concentrations in the bones, aorta, liver, lungs, kidneys, pancreas and spleen continue to increase with age (Schroeder and Tipton, 1968). While some studies have reported that this increase continues indefinitely (Barry, 1975; Barry and Mossman, 1970), others have noted a decrease in the lead burdens of many soft tissues beginning in about the eighth decade (Gross et al., 1975; Schroeder and Tipton, 1968). This decrease in soft tissue-lead levels may reflect an atrophy of parenchymal cells and an increase in interstitial matter (e.g., fascia, fat) in these tissues that has been postulated to be a part of the aging process (Gross et al., 1975; Steiglitz, 1949). Decreases in bone-lead levels may be due to osteoporosis and/or the reduced lead exposure of older persons (Gross et al., 1975).

The distribution and kinetics of lead in the body are approximated by a three-compartment model (Figure 3-1) (Rabinowitz et al., 1973; 1975). The model is based upon isotopic tracer studies of the relationships between lead intake, concentration in blood, and elimination in human subjects; consequently, the three compartments of the model represent physiological entities rather than distinct anatomical systems. Aside from blood, the majority of fluids and tissues of the body cannot be uniquely assigned to individual compartments.

The blood and certain soft tissues which exchange lead rapidly with the blood constitute compartment 1. Lead which is absorbed through the pulmonary and gastrointestinal routes enters directly into this pool and is subsequently transported within compartment 1, exchanged with either of the remaining two compartments, or eliminated in the urine. Compartment 2 accounts for a delay in the labeling of bile and other secretions relative to the labeling of


FECES
SPUTUM
ELIMINATION
90%
60%
DIET
(FOOD, WATER)
AIR
ANCILLARY SOURCES
(E.G., OCCUPATIONAL)
40%
10%
ABSORPTION
3
BONE
$T_{1/2}$ ~ 10^4 Days
94% of Body Burden
1
BLOOD
$T_{1/2}$ ~ 27-36 Days
4% of Body Burden
2
SOFT TISSUE
$T_{1/2}$ ~ 30-40 Days
2% of Body Burden
URINE
BILE, HAIR, SWEAT,
NAILS, TEETH

SOURCE: Adapted from Rabinowitz et al., 1973, 1975; Barry, 1975.

*Figures based on adult male data.

FIGURE 3-1
LEAD RETENTION: THREE-COMPARTMENT MODEL*

blood. This compartment, which contains less than half as much lead as compartment 1, is thought to represent a portion of the soft tissue not included in compartment 1 and perhaps the more actively exchanging skeletal components. Compartment 3 includes the remaining soft tissue and the majority of the skeletal material. Thus, this compartment contains most of the body burden of lead.

Of the absorbed lead which reaches the blood, about 46 percent is subsequently transferred to the other two compartments. A small fraction of the lead transferred from the blood to soft tissue is subsequently returned to the blood but the vast majority is eliminated by a variety of pathways. There appears to be no direct interchange of lead between soft tissue and bone (Rabinowitz et al., 1973).

Varying estimates of the half-lives of lead in the first two compartments have been reported in the literature: 27 and 30 days for blood and soft tissue, respectively, in a 1973 study by Rabinowitz et al.; and 36 and 40 days in a subsequent paper by the same authors (Rabinowitz et al., 1975). Regardless of this discrepancy, it is clear that the lifetimes of lead in the two compartments are quite similar. Furthermore, they are extremely short in comparison with the half-life of lead in bone, which has been estimated to be about 10^4 days (27.5 years). Thus, the body burden of lead consists of two small and highly transient pools contained in the blood and soft tissues, and a long-lived, relatively immobile fraction contained in the skeleton.

While the lead levels in the blood are quite sensitive to variations in uptake and therefore give a good indication of recent exposure, they provide little insight into a person's lifetime exposure history. Bone or dentine lead levels are a poor indicator of recent exposure but a fairly good indicator of lifetime exposure (Gross, 1976; Kehoe, 1969). An accurate chronology of lifetime lead exposure cannot be inferred from the distribution of lead in bone; however, the concentration and distribution of bone lead does provide a substantial amount of information. Because of the extremely slow turnover of compartment 3, the average concentration in this compartment more or less reflects a person's average lifetime exposure level (Barry, 1975). Furthermore, the distribution of lead within the skeleton is somewhat indicative of the nature of an individual's exposure history; soft, vascular bones such as the ribs and vertebrae contain a higher concentration of lead than dense bones such as the femur, after an acute high-level exposure, and a relatively low lead concentration following chronic low-level exposure (Kehoe, 1969).

In humans, the adverse toxicological effects of lead are associated with the mobile fraction (i.e., that which is contained in compartments 1 and 2) (NAS, 1972). The lead outputs from compartment 3 normally represent an insignificant contribution to this mobile lead; however, under certain circumstances which are not clearly understood, substantially higher quantities of skeletal lead can be remobilized. Large quantities of lead are released from bone during chelation therapy and abnormal skeletal remodeling resulting from dietary deficiencies (calcium, phosphate, magnesium) and hormonal (parathyroid hormone, calcitonin) imbalance (Bethea and Bethea, 1975; Rosen and Wexler, 1977). Lead in the soft bones is presumably remobilized more readily than lead sequestered in the dense bones (Rabinowitz et al., 1974; Rosen and Wexler, 1977).

In young children the likelihood of one of the aforementioned nutritional deficiencies (e.g., calcium deficiency) is very high. This suggests that children face an increased risk of remobilization of skeletal lead (EPA, 1977).

3.3 Elimination Characteristics

In adults, approximately 90 percent of ingested lead is eliminated in the feces without prior gastrointestinal absorption (Kehoe, 1961; Wetherill et al., 1974). The rate of absorption of lead through the gastrointestinal tract is greater in children (Section 2.1.2), who therefore eliminate a substantially smaller proportion of their total intake as unabsorbed lead in the feces.

The primary elimination route for lead absorbed by all routes is in the urine, representing about 95 percent of the total output of absorbed lead (Rabinowitz et al., 1973). Lead is excreted by the kidney into the urine, both by glomerular filtration and transtubular flow (Goyer and Mahaffey, 1972). Renal effects of lead (discussed in Section 4.1.3) may compound lead toxicity by interfering with urinary lead excretion. Direct transfer of lead to the urine takes place solely from compartment 1 (blood), and is the only direct route of excretion from this compartment.

The remaining 5 percent of the output of absorbed lead is from compartment 2 (soft tissues) in alimentary tract secretions, hair, nails, and perspiration (Rabinowitz et al., 1973). The rates and relative proportion of lead eliminated by all routes appear to be sensitive both to the dose and the chemical form of the lead, although these relationships are currently unclear (EPA, 1977).

3.4 Body Burden

A great deal of emphasis has been placed on determining the human body burden of lead, perhaps because the toxic effects of other metals, such as cadmium, are directly related to the overall body burden (Friberg et al., 1974). However, the health effects of lead do not appear to be directly related to the whole body content of lead; on the contrary, the vast majority of the lead in the body (that stored in bone) is believed to be essentially inactive (EPA, 1977). Furthermore, this inactive fraction is fairly insensitive to short-term changes in lead uptake, which directly affect health, and thus the whole body burden can provide a misleading estimate of the lead-related health hazard.

Lead is distributed differentially in the various tissues of the body. For analytical simplicity, these tissues can be grouped together on the basis of lead distribution characteristics and the body burden of lead represented as a limited number of distinct physiological compartments (such as the three-compartment model described in Section 3.2). The lead content of many or all of the tissues is in constant flux, the magnitude of which can be radically different in different tissues (Rabinowitz et al., 1973, 1974, 1975; Wetherill et al., 1974). In the compartmental model, this flux is represented by rates of input to, transfer between, and excretion from the compartment as a whole.

When the rate of lead intake is constant for extended periods (~100 days) the concentration of lead in blood reaches an approximate steady state (Wetherill et al., 1974), presumably indicating an equilibrium in the overall body burden of lead. Modifications in daily lead intake, if maintained for a sufficient length of time, will result in changes in the lead concentrations in the three compartments and the attainment of a new equilibrium condition. The rates and magnitudes of these changes are dependent upon the rates of lead flux in the tissues and can theoretically be calculated from the three-compartment model by inclusion of the appropriate parameters. Unfortunately, studies that have experimentally determined these parameters (Kopple et al., 1976; Rabinowitz et al., 1973, 1974, 1975; Wetherill et al., 1974) have used a very small number of subjects, all of whom were adult males, and a limited range of exposure conditions. Therefore, it is not certain whether these parameters are applicable to the adult male population as a whole. Furthermore, given the apparent differences in the behavior of lead in children and adults, it is almost certain that these parameters are not applicable to the child population.

4.0 TOXICITY OF LEAD

The toxicological impact of environmental lead is a cumulative product of continuous low-level exposure. The possibility that adverse health effects may result from chronic exposure from the ambient environment is of major concern.

Adverse toxicological effects are due essentially to the mobile fraction of absorbed lead within the body (EPA, 1977; Goyer and Mushak, 1977). Previously deposited fractions of lead are mobilized as a result of chelation therapy, normal skeletal remodeling and metabolism, and periods of physiological stress (Bethea and Bethea, 1975). Normal skeletal remodeling and growth is dependent upon the levels of parathyroid hormone, calcitonin, calcium, inorganic phosphate and magnesium (Rosen and Wexler, 1977). By altering the bodily concentrations of these metabolic factors, dietary metabolic imbalances (periods of physiological stress) can cause variation in the blood lead level through bone-lead mobilization.

Two properties of lead are believed to be responsible for widespread adverse health effects. Lead has an affinity for amino acids containing sulfur, resulting in deformation of protein structure. Lead also has a tendency to bind to the mitochondria, leading to interference in the regulation of oxygen transport and energy generation (Needleman and Piomelli, 1978).

Biochemical impairment of many enzyme systems has been found at very low lead exposure levels. In fact, recognition of low levels of exposure is generally a result of biochemical measurements of enzyme activities (Needleman and Piomelli, 1978). Although lead has been shown to produce enzyme interference effects at low concentrations, especially in infants and children, the amount of interference that can be tolerated by an individual without subsequent harm is uncertain. *In vitro* and *in vivo* studies have provided evidence of inhibitory effects at minute blood-lead levels (about 5 μg/dl). It is believed that a "no effect level" of enzyme inhibition by lead is nonexistent, but the physiological significance of low-level enzyme inhibition is questionable. Compensation for low lead level enzyme inhibition is thought to be achieved through a "reserve enzyme capacity" but the extent of this low level reserve capacity is as yet unclear.

A total review of the literature has not been attempted for this discussion of lead toxicity; rather, a brief synopsis is provided. More in depth discussions of the health effects of lead can be found in several publications (e.g., EPA, 1977; WHO, 1977; Kehoe, 1961; NAS, 1972).

4.1 Biological Effects Associated with Lead Absorption

Lead can affect a number of biological systems in man. The hematopoietic, nervous, and renal systems are the most sensitive to chronic low-level exposure. A number of other systems are also affected, but to a lesser degree. These include the reproductive, endocrine, hepatic, cardiovascular, immunologic and gastrointestinal systems. The discussion of health effects in this report will be limited to the three systems most sensitive to lead exposure and will focus on children. The carcinogenicity of lead compounds is also briefly discussed.

4.1.1 Hematopoietic Effects

Lead inhibits the synthesis of hemoglobin at several points throughout the heme synthetic pathway (Figure 4-1). Synthesis of hemoglobin is completed within a few days after the red blood cells enter the bloodstream; therefore, inhibition of heme synthesis must take place before this point (Guyton, 1971b). The inhibition of the enzyme δ-aminolevulinic acid dehydratase (ALAD) is believed to be the earliest known biological effect of lead intoxication (Hernberg,

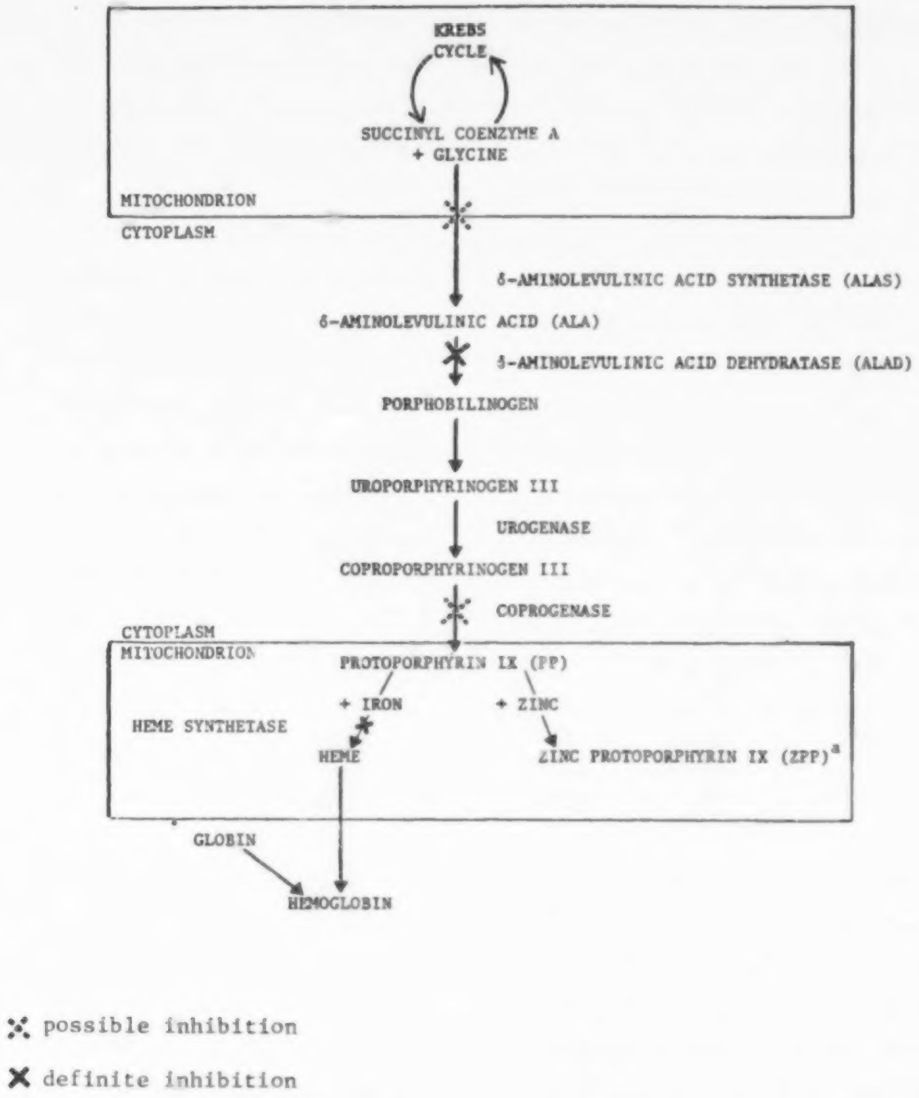

KREBS CYCLE
SUCCINYL COENZYME A
+ GLYCINE
MITOCHONDRION
CYTOPLASM
δ-AMINOLEVULINIC ACID SYNTHETASE (ALAS)
δ-AMINOLEVULINIC ACID (ALA)
δ-AMINOLEVULINIC ACID DEHYDRATASE (ALAD)
PORPHOBILINOGEN
UROPORPHYRINOGEN III
UROGENASE
COPROPORPHYRINOGEN III
COPROGENASE
CYTOPLASM
MITOCHONDRION
PROTOPORPHYRIN IX (PP)
+ IRON
+ ZINC
HEME SYNTHETASE
HEME
ZINC PROTOPORPHYRIN IX (ZPP)[a]
GLOBIN
HEMOGLOBIN
⁘ possible inhibition
✕ definite inhibition

FIGURE 4-1
SITES OF LEAD INHIBITION IN THE NORMAL PATHWAY
OF HEMOGLOBIN SYNTHESIS

[a] Precise site and mechanism of ZPP formation is unknown.

SOURCE: Adapted from Baloh, 1974; NAS, 1972.

1976). A result of this inhibition is a decline in heme synthesis due to a block in the utilization of δ-aminolevulinic acid (ALA). However, a decrease in ALAD activity has also been reported for alcoholics, diabetics, cancer patients and workers exposed to organic solvents (Yamaguchi et al., 1976) so this cannot be used as a definitive indicator of early lead toxicosis.

The degree of inhibition of ALAD activity increases with increasing blood-lead levels. Partial inhibition becomes measurable at blood-lead levels as low as 5 to 10 μg/dl (Goyer and Mushak, 1977; Chisolm, 1971; Wessel and Dominski, 1977). There is no indication that this partial inhibition is harmful since heme levels are apparently not affected. This suggests an enzyme reserve such as that discussed in Section 4.0. Above a blood-lead level of approximately 40 μg/dl, the increase in ALA excretion is exponential. The inhibition of ALAD activity accelerates as blood-lead levels increase from 40 to 80 μg/dl and higher (NAS, 1972). At blood-lead levels between 70 and 90 μg/dl, ALAD activity is almost totally inhibited (Hernberg, 1976). The relationship between blood-lead levels and ALAD activity remains constant under varying exposure conditions (i.e., new exposure, steady state, after termination of exposure) (Tola et al., 1973).

Lead also interferes with the final step in heme biosynthesis, the chelation of iron by protoporphyrin IX (PP). It is not clear whether this is due to the prevention of iron passage through the mitochondrial membrane (Needleman and Piomelli, 1978), interference with ferrochelatase activity (Lamola and Yamane, 1974), or a combination of these effects (EPA, 1977). The surplus PP created by the inhibition of iron chelation does not remain in the unchelated (free) form, but is chelated with zinc (Zn^{2+}) to form zinc protoporphyrin IX (ZPP), and bound to globin (Lamola and Yamane, 1974).

The elevated levels of PP measured in acidic solvent extracts of erythrocytes from patients with lead intoxication, led many investi-gators to the erroneous conclusion that the porphyrin present in the red blood cells of these patients was free erythrocyte protoporphyrin (FEP). However, in vivo fluorometric measurements of whole blood and isolated erythrocytes have demonstrated that the omnipresent species in lead intoxication is actually ZPP (Lamola and Yamane, 1974; Blumberg et al., 1977). This view is further supported by the fact that levels of ZPP measured in whole blood by a fluorometric technique are very similar to "FEP" levels determined by extraction methods and show an excellent linear correlation with these "FEP" values (the coefficients of correlation for linear relationships between ZPP levels and the FEP levels determined by two methods were 0.98 and 0.99) (Blumberg et al., 1977). Thus, it is thought that acidic solvents break down the ZPP chelate complex and produce the PP found in erythrocyte extracts. FEP values found in the literature have been reported as "FEP" in this study; however, it is believed that these values represent an indirect measurement of the levels of ZPP in the blood, rather than an indication of levels of free protoporphyrin IX in vivo.

Blood-lead levels in children have been associated with specific hematologic changes (Table 4-2). At 15 μg/dl there is a greater than 40 percent inhibition of ALAD activity. At 20 to 25 μg/dl, there is greater than 70 percent inhibition in ALAD activity. At 30 to 40 μg/dl, urinary excretion of ALA increases above 5 mg/l. At 20 to 25 μg/dl, there is an increase in erythrocyte protoporphyrins. At 40 to 50 μg/dl, there is a decreased hemoglobin level (Zielhuis, 1975). An increase in erythrocytic protoporphyrin is considered to be a sign of increased physiologic impairment since it is indicative of impaired mitochondrial function (WHO, 1977).

In addition to the enzymatic effects, a shortening of the life span of erythrocytes has been reported. The mechanisms responsible for the shortened life span are not clearly understood but may be the result of several physical effects. Observed effects resulting from exposure to low levels of lead include an increase in the osmatic resistance of erythrocytes, an increase in mechanical fragility and interference with a number of membrane functions, including functions which are important for maintaining cell integrity (Hernberg, 1976).

The end result of the enzymatic as well as the physical effects on the hematological system is anemia, resulting from decreased erythrocyte production and increased cell destruction. This anemia is often the earliest manifestation of chronic and acute lead poisoning and is characterized by increased numbers of reticulocytes and basophilic stippled cells in the blood. The symptoms of this anemia are pallor, waxy sallow complexion, fatigue, irritability and headache; irritabillity and decreased play activity may be signs in young children (NAS, 1972). It is believed that iron-deficient children may be more susceptible to the toxic effects of lead (NAS, 1972).

In one study, the incidence of anemia rose sharply in children as the blood-lead level increased from 37 to 100 μg/dl. At blood-lead levels below 36 μg/dl, 14 percent of the children were anemic, compared to 36 percent with levels between 37 and 60 μg/dl (Betts et al., 1973). However, the degree of anemia correlates poorly with blood-lead levels and does not become obvious until the level exceeds 80 μg/dl (Hernberg, 1976). In children, a threshold blood-lead level for anemia is about 40 μg/dl while for adults 50 μg/dl is considered the threshold level (EPA, 1977).

4.1.2 Central and Peripheral Nervous System Effects

There is a great deal of concern over the neurological effects of lead. Some segments of the population, especially children, may be exposed to lead in quantities sufficient to cause neurological and behavioral impairment, although the actual levels necessary to produce such effects are in question (EPA, 1977). It is not known whether central nervous system (CNS) impairment can occur at levels below those which produce observable effects in the hematopoietic system (Damstra, 1977).

Central Nervous System: Accumulation of lead in the body can lead to severe effects on the central nervous system. These central nervous system effects are most responsible for the morbidity and mortality associated with lead poisoning. Symptoms of neurological changes include ataxia (muscular coordination failure), clumsiness, weakness, stupor, coma and convulsions (Mahaffey, 1977).

The most severe effect of lead intoxication on the central nervous system is acute encephalopathy (degenerative brain disease). Blindness, mental retardation, behavior disorders and death can result at this level of toxicity (NAS, 1976). The pathological changes may remain after therapy (Mahaffey, 1977) and can be considered irreversible. In an early, mild form, the subclinical signs of encephalopathy include psychomotor disturbances, impairment of intelligence functions and personality changes. Massive doses of lead corresponding to blood levels above 150 μg/dl are required for the development of acute encephalopathy. As the disease worsens, cerebral edema develops (Hernberg, 1976).

Chronic exposure to lead can produce a progressive mental deterioration in children. This is characterized by loss of motor skills hyperkinetic and aggressive behavior, and convulsions, and has been associated with blood-lead levels in excess of 60 μg/dl (EPA, 1977).

There is a great deal of controversy concerning the subtle neurobehavioral effects of low-level lead exposure in asymptomatic humans. It appears that medically significant effects can be produced in adults from exposures yielding blood lead levels below 80 µg/dl. In children, lower levels (i.e., about 40 µg/dl) are believed to produce neurological damage, possibly because of the underdeveloped state of the central nervous system (EPA, 1977).

The frequency of neurologic effects appears to increase in children at blood-lead levels in the range of 50 to 60 µg/dl or above (NAS, 1976). Although this produces no major clinical effects, it has been argued that no damage to the central nervous system should be accepted. Central neruous system damage is believed to be more serious than the reversible effects on other systems since the nervous system has a poor regenerative capacity (Seppalainen et al., 1975).

Subclinical effects on intelligence and behavioral activity have been reported in children with blood-lead levels below 40 µg/dl (Goyer and Mushak, 1977). Exposure to concentrations below those levels which produce irreversible neurological dysfunctions has been postulated to be involved in the production of hyperactivity and fine motor deficits in children (Mahaffey, 1977). However, the view that these behavioral deficits are, or are related to, the cause of elevated blood-lead levels in these children is also tenable. In one study, the mean blood-lead level in 54 hyperactive children was 26.2 µg/dl while the mean blood-lead level in 37 controls was 22.2 µg/dl (David et al., 1972). Failure on fine motor tests occurred almost twice as frequently and mean IQ scores were significantly lower in children with blood-lead levels $\geq$40 µg/dl or those with blood lead $\geq$30 µg/dl having radiographically visible lead lines in the long bones than in controls (de la Burde and Choate, 1972; 1975).

Although many studies have been conducted to test low-level lead effects on the CNS, no conclusive evidence has been presented. It remains unknown whether psychological, emotional and neurological sequelae occur in asymptomatic children with blood-lead levels below those associated with clinical lead poisoning.

Peripheral Nervous System: In addition to the effects on the central nervous system, peripheral neuropathy due to lead poisoning has been reported. Peripheral nervous system paralysis is characterized by selective involvement of motor neurons and is manifested as weakness of the extensor muscles. At blood-lead levels of 80 to 120 µg/dl, a slowing of the conduction velocity of the nerves of the upper limbs and electromyographic abnormalities have been reported (Hernberg, 1976).

Although peripheral neuropathy is considered rare in childhood lead poisoning, it has been suggested that this is because the effects are overshadowed by the clinical symptoms of encephalopathy. Feldman et al. (1973) observed a statistically significant ($p < 0.002$) decrease in peripheral nerve conduction velocity in a group of 24 children with blood-lead levels of 40 µg/dl or greater. In studies involving lead workers with mean blood-lead levels of 40 ± 9 µg/dl, a slowdown of nerve conduction velocity in the upper extremities and electromyographic abnormalities (i.e., fibrillations and diminished number of motor units on maximal contraction) were reported (Seppalainen et al., 1975).

4.1.3 Renal Effects

There appear to be two distinct renal effects from chronic lead exposure, reversible proximal tubular damage and progressive, irreversible renal failure. Although dose-response relationships have not been defined, it appears that the effects occur only at levels above those which affect heme synthesis (Hammond, 1977).

Renal tubular dysfunction is manifested in children as Fanconi's syndrome, characterized by glycosuria (presence of abnormal amounts of glucose in urine), hypophosphatemia (an abnormally decreased amount of phosphate in the blood) and aminoaciduria (presence of amino acids in the urine). Aminoaciduria reportedly results from blood-lead levels above 80 μg/dl (Chisolm, 1962); however, the exact level which produces this effect is unclear. The Fanconi syndrome has been reported in one-third of the children in one study with acute encephalopathy and blood-lead levels above 150 μg/dl (NAS, 1972).

Studies indicate that chronic kidney damage is the result of high renal lead content for long periods of time. There is no evidence to suggest that kidney damage occurs in asymptomatic cases; effects only occur in association with other symptoms of lead toxicity (Damstra, 1977).

Prolonged and excessive exposure to lead can result in chronic lead nephropathy, although the level of exposure which causes this effect is not known (Hammond, 1977). Chronic lead nephropathy, a progressive and irreversible disease, is characterized by progressive azotemia (presence of urea in the blood), interstitial fibrosis, tubular degeneration and glomerular vascular changes in small arteries and arterioles of the kidney (Morgan et al., 1966). Renal insufficiency may be a sign of subclinical lead poisoning (Campbell et al., 1977). Renal failure may result from more extensive exposure (EPA, 1977).

The formation of inclusion bodies, composed of a lead-protein complex containing approximately 50 μg lead/mg protein (Moore et al., 1973), is one of the earliest effects of lead nephropathy (Hernberg, 1976). These inclusion bodies appear in renal proximal tubular cells as well as in other tissues (Hammond, 1977). The lead in the inclusion bodies is 60 to 100 times more concentrated than in the whole kidney (Goyer and Mushak, 1977). These inclusion bodies may serve as a defense mechanism by binding the lead and thus lowering the concentration of lead in the cytoplasm (Goyer and Chisolm, 1972).

Chronic renal injury from lead exposure can also produce gout (Emmerson, 1968). Although the mechanism of interference with uric acid excretion is not known, it has been hypothesized that the rise in the serum urea level may result from a loss of glomeruli, leading to a reduction in the glomerular filtration rate (Campbell et al., 1977).

High levels of lead in drinking water (>100 μg/l) have reportedly been responsible for renal failure, hyperuricemia and gout in individuals drinking the water for 15 to 30 years (Beattie et al., 1972).

4.1.4 Carcinogenicity

A relationship between lead exposure and cancer in humans has not been demonstrated. However, very high doses of lead salts have been shown to be carcinogenic in laboratory animals by a number of investigators: lead phosphate in rats (Zollinger, 1953; Roe et al., 1965; Sunderman, 1971) and mice (Sunderman, 1971); lead acetate in rats (Boyland et al., 1962; Zawirska and Medras, 1968; Kanisawa and Schroeder, 1969; Sunderman, 1971; Coogan, 1973; Stiller, 1973) and mice (Van Esch and Kroes, 1969; Sunderman, 1971); and lead subacetate in rats (Van Esch et al., 1962; Mao and Molnar, 1967; Oyasu et al., 1970; Sunderman, 1971) and mice (Van Esch and Kroes, 1969). Tumors of the kidney, both benign and malignant, were produced in all of these studies, regardless of the route of administration (orally in food or water, or by intraperitoneal and/or subcutaneous injection). High incidences of tumors of the testes, adrenal, thyroid, pituitary, prostate and lung have also been seen in rats and mice receiving these salts (Zawirska and Medras, 1968; Sunderman, 1971), and cerebral gliomas have been observed in 2 rats out of 17 receiving dietary lead subacetate (Oyasu et al., 1970).

In contrast to the animal data, no significant relationship between exposure to lead and cancer in a human population has been reported. Dingwall-Fordyce and Lane (1963) conducted a follow-up study of 425 persons who had been exposed to lead in a storage battery factory. No evidence was found to suggest a correlation between lead absorption and malignant disease. In a more recent study (Cooper and Gaffey, 1975; Cooper, 1978), the incidence of death from malignant neoplasms among battery plant workers and from lung cancer among smelter and battery plant workers was slightly higher than expected, although this increase was not statistically significant.

A consistent feature of the animal studies is that the animals were subjected to very large quantities of the lead salts utilized. The lowest dietary concentration of a lead salt which produced cancer in the feeding studies was 0.1 percent. In the injection studies, the lowest lifetime dose received by rats that developed renal tumors was 120 mg. IARC (1972) noted that the level of human exposure equivalent to the intake of lead acetate that has produced renal tumors in rats is 810 mg/day (550 mg Pb/day). This level greatly exceeds that at which severe, debilitating effects and even death will be produced. Thus, even if lead is a human carcinogen, the carcinogenic effects will presumably be greatly overshadowed by the systemic toxic effects at the exposure levels generally encountered. Carcinogenicity cannot be considered a singular risk associated with lead exposure since the systemic effects constitute a major public health problem.

4.2 Indices of Exposure/Effect

There are many tests which can be used for the detection of increased lead absorption. Tests which measure both tissue lead content and tissue metabolic effects are available. However, no single test can be used for the determination of body burden or total metabolic effects. At present, blood-lead concentration is considered the best available measure of tissue lead content, while free erythrocyte protoporphyrin (FEP) concentration is the best measure of tissue metabolic effects (Baloh, 1974).

4.2.1 Lead Levels in Tissues

The concentration of lead in several tissues has been used to indicate an individual's past exposure history to lead. Although blood-lead content is the most widely used criterion, tissues, urine, hair, teeth and bone have been sampled.

Blood Lead: The blood-lead level is used both as an index of exposure and for the diagnosis of health effects. This value is the most widely accepted measure of recent exposure, as well as representative of the actual mobilized fraction of lead responsible for the toxic effects in the body (Goyer and Mushak, 1977). A blood-lead level of 40 μg/dl is believed to be the maximum level at which no adverse health effects are found, although changes in enzyme activity have been observed below this value. Clinical manifestations of lead poisoning begin when blood-lead levels are consistently above 80 μg/dl (Goyer and Mushak, 1977; NAS, 1976).

Five methods are commonly used for the determination of blood-lead concentrations: spectrophotometry, flame atomic absorption, Delves cup, furnace atomic absorption, and anodic stripping voltammetry. These methods reportedly have the capability of producing results which are valid and reproducible within 5 percent precision or better. However, interlaboratory comparisons do not appear to confirm this degree of reproducibility. Discussions of the methods (Pierce et al., 1976) and the variability of the results of the methods (Lucas, 1977) have recently appeared in the literature. There are many sources of variability involved, including sampling technique, storage time, contamination, and analytical procedure (Pierce et al., 1976). Studies indicate that up to 80 percent of the variability can be due to analytical method error (Lucas, 1977). Because of the wide variation in blood-lead measurements, it is common practice to run at least two analyses of the same blood sample.

Even with these limitations, blood-lead analysis is still the most widely used test for the diagnosis of increased lead absorption. Many of the other test methods are based on a relationship to blood lead.

Urine Lead: Both blood-lead and urine-lead levels are accurate indicators of recent lead exposure. Urine-lead levels are considered less accurate in that they are susceptible to changing renal output or to dilution due to variable water content. In a steady state, urine lead is representative of blood lead.

A "normal" value for urinary lead in young children is usually less than 55 μg/24 hours. However, this value should not be used as an index of body burden since there can be complicating factors that affect lead excretion and give a false impression of the amout of lead in the body (Baloh, 1974).

Hair Lead: Hair lead analysis can be easily performed and can indicate chronic lead exposure. Since lead reacts with the sulfhydryl groups in hair protein as the hair emerges from the scalp, the concentration of lead at different sections can be indicative of episodic exposures to high lead levels (Goyer and Mushak, 1977).

Contamination of hair by exogenous deposition poses a problem in evaluating the measurement. Although mean levels in children and adults are in the range of 20 to 30 μg/g hair (Baloh, 1974), appropriate precautions (e.g., careful washing of the hair sample) must be taken if the measurement is to be considered a reasonable indicator of exposure.

Tooth Lead: Tooth lead analyses have been used to a limited degree as indicators of past heavy lead exposure. It is believed that the lead content of the tooth represents the total exposure up to the time of removal. The reliability of tooth lead concentrations as an indicator of lead toxicity has not been evaluated (Baloh, 1974).

Bone Lead: Bone is an ideal tissue to analyze for total body burden measurement, since more than 90 percent of the body burden of lead is deposited in the skeletal system of adults, and 60 to 65 percent is deposited in the bone tissue of children. However, the value of such a determination is questionable since this bound lead is very slowly mobilized and does not represent a great danger. Correlation of bone-lead levels to the manifestations of toxic symptoms cannot be made, although bone-lead levels may single out those individuals highly susceptible to lead toxicity (Goyer and Mushak, 1977). Multiple bands of increased density in growing long bones (as seen by radiographic examination) indicate prolonged, increased absorption of lead (NAS, 1972).

4.2.2 Metabolic Effects Associated with Lead in Various Tissues

It appears from the literature that there is a trend toward putting more reliance on measurements of metabolic effects associated with absorbed lead in tissues rather than on blood-lead values. While the blood-lead level is considered a reliable index of recent lead exposure, it does not necessarily indicate the extent of lead-induced toxic effects. For this reason, considerable attention has been focused on measurements of the levels of intermediates and enzymes of the heme-synthetic pathway in the blood. Variability associated with blood-lead measurements has provided additional impetus for finding direct indices of lead toxicity. However, until these new methods have been tested and approved, blood-lead values will continue to be the most widely used measurement. Some of the tissue metabolic effects measurements have been correlated with blood-lead values. A table (Table 4-1) showing these reported associations follows the discussion.

Tissue effects measurements include free erythrocyte protoporphyrin (FEP) and zinc protoporphyrin (ZPP) determinations, urine coproporphyrin (COPRO) measurement, urine δ-aminolevulinic acid (ALA) determination, and δ-aminolevulinic acid dehydratase (ALAD) activity measurements. These determinations are useful in detecting the subclinical effects of lead on hemoglobin synthesis. Since lead inhibits several enzymes essential to the synthesis of heme, measurement of heme precursors in the blood and urine can be indicative of metabolic effects associated with increased lead absorption.

Zinc Protoporphyrin/Free Erythrocyte Protoporphyrin: Zinc protoporphyrin (ZPP) appears in the blood as a result of chronic lead absorption. Since ZPP fluoresces when excited with high energy blue light, the compound can be fluorometrically assayed. A rapid and reliable test for lead absorption based on this assay has been devised. This test can differentiate between lead poisoning, iron-deficiency anemia, and other disorders which may cause a rise in ZPP levels (Lamola et al., 1975a,b).

Numerous investigators have reported levels of "free erythrocyte protoporphyrin" (FEP) based upon measurements of free protoporphyrin IX (PP) in acidic solvent extracts of whole blood and isolated erythrocytes. However, the presence of PP in these extracts is apparently a secondary effect of the extraction procedure on the ZPP present in the erythrocytes (Section 4.1.1), and therefore FEP is thought to be an indirect measurement of ZPP (Lamola and Yamane, 1974).

A recent development has been the design of a portable hematofluorometer which can, in about five seconds, measure ZPP concentrations under field or laboratory conditions from a single drop of whole, unprepared blood. This appears to be a highly effective and efficient means of detecting the early signs of lead absorption and

and could be useful as a mass screening technique. A discussion of this instrument has recently appeared in the literature (Blumberg et al., 1977).

Urine Coproporphyrin: Coproporphyrin (COPRO) measurements are considered less specific than FEP measurements. Coproporphyrin excretion begins to increase at approximately 35 to 40 μg/dl blood-lead levels, but can be affected by conditions other than lead exposure. Hepatic disorders, rheumatic fever, poliomyelitis, infectious mononucleosis, and alcoholism can all increase the COPRO level in urine (Baloh, 1974).

Both sample collection and analysis of the COPRO test are simple. An approximate upper bound to the normal excretion rate for both adults and children is 0.2 μg/ml urine (Baloh, 1974).

δ-Aminolevulinic Acid: Increased levels of δ-aminolevulinic acid (ALA) in urine have been associated with blood-lead levels of 40 to 50 μg/dl in adults (Hernberg et al., 1970). Since levels of concern can be below this, the concentration of ALA in urine is of limited utility. An upper normal level of excretion is difficult to define. Since the rate of both false negatives and false positives is high, the ALA test is not recommended for mass screening programs.

δ-Aminolevulinic Acid Dehydratase: A more sensitive index of low level lead absorption is ALAD activity. This test can detect changes in lead concentrations down to blood-lead levels of approximately 5 μg/dl (Hernberg et al., 1970). This test is believed to be the most sensitive indicator of biological effect. It has the advantage of showing changes in lead absorption in asymptomatic humans (Goyer and Mushak, 1977). Although partial inhibition of ALAD activity does not cause any adverse health effects, presumably due to a large reserve capacity, it is reflective of early biochemical alterations at low ambient environmental levels (Hernberg, 1976).

The correlation of ALAD to blood-lead level is very good (Tola et al., 1973). Because of this close agreement, ALAD can be used to predict blood-lead values.

4.2.3 Other Indices

Although not useful for monitoring or screening purposes, other indices can be used to assess lead absorption. Nerve-conduction velocity measurement can be a useful neurological test to detect early signs of lead exposure (Seppalainen et al., 1975; Singerman, 1976). Renal function tests and electron microscopic examination of the characteristic inclusion bodies are other possible measures of lead exposure (Task Group on Metal Toxicity, 1976). However, since renal function and nervous system damage are not evident before clinical symptoms appear, the determination of hematological changes remains a more useful tool for early detection of exposure (Singerman, 1976).

4.3 Effects Levels

Specific toxic effects of recent lead exposure in humans are characteristic of exposure levels. These effects levels can be measured by many physiological indicators. Blood-lead levels are the most commonly reported index of the extent of recent lead exposure and of the active toxic fraction of lead in the body.

There is a positive correlation between blood-lead levels of $\geq$ 80 μg/dl in adults and anemia and neurological impairment. Similar effects are seen in children with blood-lead levels of $\geq$ 50 to 60 μg/dl (NAS, 1976). The more subtle manifestations of subclinical behavioral dysfunction (e.g., hyperactivity, slowed learning ability) are not directly measurable by neurochemical tests, but are estimated with functional tests and correlated with hematopoietic chemical

TABLE 4-1

CORRELATION BETWEEN BLOOD LEAD AND OTHER TESTS

TEST	RELATIONSHIP	REFERENCE
ZPP	log ZPP (μg/dl Blood)=0.54 + 0.017PbB (μg/dl Blood) (r = 0.77)	(Adults; Lamola et al., 1975b).
ZPP	log ZPP (μg/dl Blood)=0.52 + 0.027PbB (μg/dl Blood) (r = 0.87)	(Children; Lamola et al., 1975b).
ALAD	log ALAD (units/ml RBC)=2.274 - 0.018PbB (μg/dl Blood) (r = 0.9)	(Hernberg et al., 1970)

measurements of the hemoglobin enzyme system. Since blood oxygen-carrying capacity is effectively lowered with the onset of the inhibition of heme production, CNS degradation is expected to parallel heme inhibition, because of the extreme sensitivity of the CNS to hypoxia.

In vivo and _in vitro_ studies reveal inhibition of ALAD at levels as low as 5 μg/dl (Hernberg et al., 1970; Chisolm et al., 1975), but it is believed that there is no complete absence of the enzyme-inhibitory effect of lead at any level (Wessel and Dominski, 1977). This may be compensated for at low lead levels by a reserve enzyme capacity, but the individual effective range of this reserve is as yet unclear. Despite this possible reserve, blood-lead levels of 30 μg/dl in women have resulted in definite ALAD inhibition (Hernberg et al., 1970).

Table 4-2 presents a sample of the reported known low blood-lead level and acute high blood-lead level effects.

TABLE 4-2

CLINICAL SIGNS OF LEAD INTOXICATION

Pb-Blood Level (µg/dl)	Effect	Reference
5-20	• Normal background levels	King (1971); Jenkins (1976)
	• Partial inhibition of ALAD activity but no measurable increase in ALA excretion	Jenkins (1976)
15	• Threshold level for increase in EP.	Piomelli (1978)
25-30	• Increase in protoporphyrin concentration in women and children	Hernberg (1976); NAS (1976)
	• Deleterious effects on red blood cells (change in osmotic resistance and mechanical fragility)	Hernberg (1976)
	• FEP elevation of diagnostic importance	Piomelli et al. (1973)
30-50	• Potential danger to children	Center for Disease Control (1975)
	• First detectable increase in ALA excretion and FEP levels in body fluids; anemia	Jenkins (1976)
	• Increase in protoporphyrin concentration in men	Hernberg (1976)
	• Decreased ALAD activity	Goyer and Mushak (1977)
40-80	• Decreased ALAD activity	Goyer and Mushak (1977)
	• Increase in urinary ALA, CP	Goyer and Mushak (1977)
	• Increase in FEP	Goyer and Mushak (1977)
	• Reticulocytosis	Goyer and Mushak (1977)
	• Nerve conduction effects	Goyer and Mushak (1977)
	• Inclusion bodies	Goyer and Mushak (1977)
	• Adverse metabolic effects on heme synthesis, early mild symptoms of plumbism	Jenkins (1976); NAS (1976)
	• Slight drop in hemoglobin level	NAS (1976)
	• Anemia	NAS (1976)

TABLE 4-2 (CONCLUDED)

Pb-Blood Level (μg/dl)	Effect	Reference
	• Increased risk of acute and chronic clinical effects	NAS (1976)
	• Obvious anemia	NAS (1976)
	• Reticulocytosis becomes measurable	Hernberg (1976)
	• Shortening of erythrocyte life span	Hernberg (1976)
>80	• Decreased ALAD activity	Goyer and Mushak (1977)
	• Fivefold increase in urinary ALA, CP	Goyer and Mushak (1977)
	• Increase in FEP	Goyer and Mushak (1977)
	• Anemia	Goyer and Mushak (1977)
	• Ataxia, coma, convulsions	Goyer and Mushak (1977)
	• Fanconi syndrome, chronic nephropathy	Goyer and Mushak (1977)
	• Acute neurological disorders	Goyer and Mushak (1977)

5.0 SENSITIVE POPULATIONS

Two subgroups within the general population have been identified as more sensitive and at greater risk to environmental lead exposure than the average adult. Children under the age of four are especially susceptible to the toxic effects of lead. Fetuses have also been identified as a sensitive population and the pregnant female as their exposure vehicle based on the fact that the fetus is exposed to lead via transplacental absorption.

5.1 Children

Children are known to be especially susceptible to acute and chronic lead poisoning. Empirical evidence indicates that children tend to become exposed to and absorb greater quantities of lead than do adults. In addition, clinical studies demonstrate that young children are much more likely to suffer ill effects from lead exposure than adults. The following paragraphs support the contention that children (from 1 to about 4 years of age) should be considered the critical receptor to environmental lead exposure and that regulatory actions should incorporate suitable safety factors during standard-setting procedures.

5.1.1 Increased Potential for Exposure to Lead

There is an increased hazard to children from the ingestion of lead-contaminated materials. Normal hand-to-mouth activity (i.e., thumb sucking and finger licking) in young children is a significant mechanism of lead exposure. Lead contaminated soil and dust is a primary exposure source for children due to this activity (Lepow et al., 1974). Juvenile dietary habits are responsible for additional exposure to lead. These immature dietary habits include the retrieval and ingestion of dirt- or dust-contaminated foodstuffs (Day et al., 1975).

In addition, there is significant opportunity for increased lead exposure among children with pica and among children who mouth foreign objects. Pica, the repetitive ingestion of nonfood items, is a fairly common behavior pattern among young children. Two studies (Millican et al., 1962; Barltrop, 1966) have described the incidence of pica and mouthing behavior in child populations. In both studies, the incidence rates for pica and mouthing were highest in the youngest children studied (1 to 2 years) and decreased fairly steadily until 3 to 4 years of age. In addition, both studies reported that the incidence of these behaviors (particularly pica) in black children was generally substantially higher than in white children of the same age. Social, cultural, and economic differences between the populations almost certainly contributed to this difference. Thus a physiological etiology for the difference in incidence rates could not be inferred from these investigations. Among white children 1 to 2 years old, 28 percent had pica and about 82 percent displayed mouthing behavior; among blacks the rates were 57 and 78 percent for pica and mouthing, respectively (Millican et al., 1962). Among children 2 to 3 years old the rates were 20 and 52 percent for white children and 40 and 62 percent for blacks. The prevalence of pica among white children was low after age 3 (2 to 4 percent), but among black children it remained at about 20 percent up to age 6 (Millican et al., 1962).

Estimates of lead intake by children with pica for paint range as high as 2.1 mg/day (NAS, 1976), about ten times greater than what one might expect from normal environmental sources (i.e., 100 to 200 µg/day from air, food, and water). Due to the variables involved (e.g., housing, socioeconomic condition), it is difficult to quantify the additional lead intake by children with pica, for the infant population in general, or for specific subsets within that population. It is obvious, however, that in certain instances, children with pica for paint can absorb lead in amounts significantly greater than normal.

Respiratory characteristics of the child impose a greater potential for inhalation of airborne lead than those of the adult. Children take part in greater physical activity than adults, thereby increasing their air intake, and breathe more through the mouth (due to greater physical activity and more frequent respiratory infections) thus employing a less effective filtering mechanism (American Lung Association, 1978).

The child has an enhanced risk of exposure to lead via inhalation since concentration gradients for airborne lead increase as one approaches ground level (Jenkins, 1976). Vehicular exhaust, a low altitude source of airborne particulate lead, is a major contributor to the inhaled component of lead uptake in the child living in close proximity to heavily trafficked areas (NAS, 1972; Angle and McIntire, 1975). The child is also exposed to lead from dust that is resuspended by vehicular traffic (Jenkins, 1976). Resuspension is dependent upon vehicle speed. A range of 1 to 5 percent resuspension of deposited particulates by passing vehicles has been estimated (Sehmel, 1976).

5.1.2 Metabolic Differences

Children appear to have a gastrointestinal lead absorption rate that is four to five times higher than that of adults (Mahaffey, 1977; Alexander, 1974; NAS, 1976). This increased absorption rate, coupled with the potentially higher exposure dose (as a result of pica) can result in much higher blood-lead levels than expected in an adult.

The daily uptake per unit body weight in children far exceeds that in adults. It should be noted that the studies showing roughly equivalent blood-lead concentrations in children and adults do not necessarily refute this point, since a child may be able to assimilate blood lead into the soft tissues and bone at a more rapid rate than an adult (Jenkins, 1976).

The relative proportion of the lead body burden in the slow exchange pool (i.e., in the dense bone matrix) is smaller in children than in adults. Only 60 to 75 percent of the lead body burden is located within a child's skeletal system, compared to 90 percent or more in the adult (Barry, 1975; EPA, 1977). This suggests that a larger amount of the absorbed lead can be concentrated in the soft tissues, where it may reach toxic concentrations. For example, brain tissue in neonatal rat tends to concentrate lead to a greater degree than in adults (NAS, 1976).

Mechanisms for elimination of heavy metals are not well developed in the young, and this may ultimately result in higher soft tissue lead burdens in children than in adults at the same rate of lead uptake (per unit body mass). Studies have indicated that blood-lead levels in immature and adult rats were comparable after acute lead exposure, but were sustained longer in the immature rat (Bayley and Brown, 1974).

5.1.3 Inherent Physiological Sensitivity

Studies in both laboratory animals and children have shown that the brain is highly vulnerable to irreversible damage during infancy and early childhood because of rapid growth rate of this organ (NAS, 1976). Due to this immature developmental state, infants may be especially sensitive to the detrimental effects of lead exposure.

The infant's higher susceptibility is due in part to the rapid growth rate characteristic of organogenesis. Organ formation occurs from the second trimester of pregnancy through the fourth year postpartum. This period of rapid growth and increased stress sensitivity is considered the "growth spurt" (NAS, 1976).

In humans the growth spurt is defined in terms of three brain components. Glial replication and differentiation continue through the first eighteen months after birth. Myelination extends through the third and fourth years. Cerebellar growth extends through the eighteenth month postpartum and is most rapid during this period (NAS, 1976). This rapid growth rate increases susceptibility to a variety of stresses such as nutritional deficiencies. Studies of infants with pyloric stenosis have shown that the brief starvation period encountered had permanent effects on their learning abilities and general adjustment ability 5 to 14 years later (Klein et al., 1975). Reduced IQ levels have been demonstrated in school age children who had experienced malnourishment during the initial two years postpartum (NAS, 1976).

Long-term behavioral deficits were demonstrated in neonatal rats receiving oral administration of lead (Sabotka and Cook, 1974). Study groups of asymptomatic children with a history of pica for paint displayed poor learning ability, seizures, and hyperactivity (de la Burde and Choate, 1972). Similar findings are reported for symptomatic children (Byers and Lord, 1943).

5.2 The Fetus and Pregnant Woman

Physiological sensitivity to lead may be at a maximum during fetal development. The pregnant female must be recognized as the exposure vehicle for the fetus since the placental transfer of lead is the main route of fetal lead uptake. In addition, the pregnant female may herself be more sensitive to lead due to increased food intake and changes in hormonal status. Hormonal imbalances which result from pregnancy (Guyton, 1971a) may influence the mobilization of lead from bone.

5.2.1 Placental Transfer

Lead has been shown to cross the placental barrier in laboratory animals (Kostial and Momcilovic, 1974; McClain and Siekierka, 1975) as well as in humans (Baglan et al., 1974; Gershanik et al., 1974). There does not appear to be any significant difference between maternal and fetal blood-lead levels at any time during pregnancy

(Gershanik et al., 1974), although placental blood-lead levels may be slightly (but not significantly) higher than levels in maternal or fetal blood (Baglan et al., 1974; Harris and Holley, 1972). Lead has been detected in the fetus as early as the twelfth week of intrauterine life and has been shown to increase throughout gestation. The lead content of the fetus at birth has been recorded as 300 μg; the equivalent of the daily intake for the normal adult (Barltrop, 1977).

The transplacental passage of lead in blood is particularly important for two reasons. The fetus is highly sensitive to the neurological effects of lead exposure (due to lack of blood-brain barrier, efficient absorption, and rapid brain growth rates). Additionally, the newborn is starting life with a significant "background" blood-lead level. The observed positive correlation of urinary ALA levels with blood-lead levels in newborns indicates that heme-biosynthetic derangement must have begun in utero (EPA, 1977). Exposure of pregnant women to high water-lead concentrations has been correlated with the higher blood-lead concentrations in their mentally retarded offspring (Moore et al., 1977). This reinforces the association between lead exposure during pregnancy and subsequent neurological damage to the fetus, but the specific exposure, absorption, and retention levels and their corresponding specific effects are as yet unknown.

5.2.2 Inherent Sensitivity: Immature Organogenesis

The fetus displays an immature developmental state, as well as a lack of development of a blood-brain barrier (Bridbord, 1978). The uptake (absorption) of lead has been shown to be six to eight times greater in the brain of suckling rats than in the brain of adult rats (Momcilovic and Kostial, 1974). Krigman and Hogan (1974) observed a fourfold increase of lead uptake in the brain of suckling rats as compared to adults. The immature state of the fetal brain, central nervous system, and elimination systems results in increased sensitivity to very low concentrations of lead. In humans, neurological development seems most pronounced from the second trimester of pregnancy until several years after birth (NAS, 1976). Permanent neurological damage may result if the individual is stressed during this sensitive span. The lack of development of the blood-brain barrier, in combination with the increased permeability of cerebral capillaries in the fetus, amplifies the sensitive state already created by immature brain-tissue development. Thus, while the brain and central nervous system of the fetus are inherently sensitive to concentrations which are nontoxic to mature systems, they are also prone to increased deposition of lead.

Rapid brain growth rates of infants create a greater risk of lead-induced neurologic damage. This rapid growth rate takes the form of the growth spurt in humans, occurring during the second trimester of pregnancy, through the initial four years postpartum. Permanent adverse effects on learning ability can result from the impact of lead on the brain during this growth spurt (NAS, 1976). Behavioral abnormalities (i.e., hyperactivity, aggressiveness, tremors and repetitive grooming behavior), have been produced in rats exposed to lead during the growth spurt period (Michaelson and Sauerhoff, 1974). Suckling rats fed maternal milk dosed with lead during postnatal days 1 through 10 showed significantly slower learning than those fed equal doses of lead during days 11 through 21 (Brown, 1975).

5.3 Threshold Levels

Threshold-lead levels are defined as those minimum blood-lead levels capable of inducing toxic response. In attempting to define a safe threshold level in terms of blood-lead levels, the most physiologically receptive (sensitive) population to augmentations in this level must be singled out and labeled as the highest risk group. The maximum safe threshold level must also accommodate variations in individual responsiveness to this lead level.

Due to higher lead absorption rates, unique sources of exposure and lack of mature development of excretory systems (yielding higher pooling in target tissues), fetuses and young children are the most physiologically receptive and sensitive individuals. Therefore, in defining a threshold level for lead, the lowest known toxic levels affecting this portion of the human population should be used. A suitable margin of safety must be incorporated into the determined threshold toxic effects level when setting any environmental standard. A conservative margin of safety should be employed in defining the allowable limits of exposure for the developing fetal central nervous system due to the proven neurotoxicity of lead (EPA, 1972a).

ZPP elevation and corresponding impairment of heme synthesis at blood-lead levels above 30 μg/dl are regarded as unsafe for children and unacceptable by EPA (1978b). There are, however, contrasting opinions as to the actual impact of a rise in ZPP levels. ZPP elevation may not indicate insufficient heme or hemoglobin production, although it does indicate an interference in the heme synthetic pathway. The rise in ZPP may be caused by other factors such as iron deficiency (EPA, 1978b).

The Center for Disease Control (1975) set the level of significant danger to children at 30 μg/dl, and considered FEP levels to be of significant diagnostic importance. The level of 30 μg/dl set by the CDC is endorsed by the American Academy of Pediatrics and is now the target level set by EPA (1977) at which undue lead exposure begins.

Although the maximum safe lead level has been set at 30 μg/dl by CDC, retrospective studies indicate that hyperactivity and altered motor activity may be correlated with blood-lead levels in children having blood-lead levels lower than 30 μg/dl. These studies suggest that blood-lead values in the 25 to 30 μg/dl range may initiate toxic effects in children but this position is based on the tentative hypothesis that lead is the cause of hyperactivity and altered motor activity in these children; in fact, this behavior may be the cause of or be correlated with the cause of the elevated blood-lead levels. Increased FEP levels have been recorded in women and children at the 25 to 30 μg/dl level (NAS, 1976; Zeilhuis, 1975).

6.0 SOURCE CONTRIBUTIONS TO DAILY LEAD UPTAKE IN HUMANS

The method employed in this study to estimate the degree to which each major environmental source of lead exposure contributes to an individual's total daily lead uptake is based on probable exposure conditions (i.e., ambient lead levels) as well as individual biological absorption rates for each exposure route. The method consists of a five-step process:

- definition of ambient concentrations of lead for the major exposure sources (i.e., air, food, drinking water, soil/dust, paint)

- determination of daily lead intake according to the relationship:

  $$I_i = C_i \cdot [Pb]_i$$

  where I_i is the daily lead intake from source i (e.g., air, food, drinking water, paint, soil/dust), C_i is the consumption per day of each lead source i and $[Pb]_i$ is the concentration of lead in each source i

- calculation of the amount of lead absorbed from each exposure source i:

  $$U_i = I_i \cdot A_i$$

  where U_i is lead uptake for each exposure source i, I_i is the daily lead intake from each source i, and A_i is the percent absorption of lead, via the appropriate exposure route, for the particular source.

- calculation of the total lead uptake from all sources, U_t:

  $$U_t = \Sigma(I_i \cdot A_i) = \Sigma U_i$$

- determination of the proportion (P_i) of total daily uptake (U_t) provided by each of the five possible exposure sources (i.e., source contribution factors):

  $$P_i = \frac{U_i}{U_t} \cdot 100$$

6.1 Basic Assumptions

Certain assumptions are required to define the amount of each source material consumed per day. Where appropriate, Reference Man* values are utilized for daily air and food consumption rates (see Table 6-1). Daily consumption rates for drinking water are those values suggested by NAS (1977) as conservative estimates.

Hand-to-mouth activity (e.g., thumb sucking and finger licking) resulting in the ingestion of soil/dust is a normal behavioral characteristic of children through five years of age (Piomelli, 1978). Within a lead-contaminated environment, hand-to-mouth activity and immature dietary habits (i.e., the retrieval of food from dusty surfaces or soil, and subsequent consumption), make soil/dust a major source of ingested lead for children. Under average urban conditions (after thirty minutes of normal playground activity) 5 to 50 mg of dirt from a child's hand can be transferred to a typical "sticky sweet." Ingestion of 2 to 20 sweets could result in an intake of 100 mg of soil/dust or more (Day et al., 1975). A small child playing in dirt easily ingests 10 mg of soil/dust with each episode of hand-to-mouth activity. A conservative estimate of ten hand-to-mouth activitites a day would result in the ingestion of 100 mg of soil/dust a day (Lepow et al., 1974). Therefore, 100 mg per day would seem to be a reasonably conservative assumption for the ingested soil/dust of the two- to three-year-old.

Pica occurs to some degree in a substantial percentage of children between 12 and 36 months of age (NAS, 1976). Children exhibiting pica for paint are of major concern, because of the high levels of lead in some paints, with older painted surfaces containing lead in concentrations greater than 1 percent. Pica for paint is believed

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*From the ICRP Reference Man tables (International Committee on Radiological Protection [ICRP], 1975).

TABLE 6-1

BASIC ASSUMPTIONS EMPLOYED IN THE
CALCULATION OF INDIVIDUAL SOURCE CONTRIBUTION FACTORS

BASIC ASSUMPTIONS	LEVEL	REMARKS
• Reference Man:		
Adult consumes:	2.0 liters H_2O/day	- Daily intake as suggested by NAS (1977); conservative estimate, since all beverages assumed to be water, which has higher [Pb] than generic beverages (See Table 2-3).
	~2200g food/day	- Approximate daily intake for 18-yr old in FDA total diet studies; comparable to Reference Man (ICRP, 1975).
	22.8 m^3 air/day	- Assumes 8 hrs light work, 8 hrs nonoccupational, and 8 hrs resting (ICRP, 1975),
• Pregnant female:	2.0 liters H_2O/day 2200g food/day 21.1 m^3 air/day	
Child consumes:	1.4 liters H_2O/day	- Conservative estimate for 2-yr old child, <2-yr old assumed to obtain liquid from foods alone
	~1000g food/day	- Approximate daily intake for child from FDA total diet studies
	4.7 m^3 air/day	- For 2-yr old; based on ICRP (1975) values for newborn, one-,10-, and 18-yr olds.
	100 mg soil and dust/day	- Conservative estimate for normal hand-to-mouth activity in children (Lepow et al., 1974)
	142 mg paint/day	- Conservative estimate for children with pica (NAS, 1976)
• Absorption Characteristics:		
Gastrointestinal		
Adult	10%	- See Table 3-2; generally recognized approximation
Child	50% for food and water	- See Table 3-2; (NAS, 1976; EPA, 1972a)
	30% for soil/dust	- Estimate based on compromise between food and paint absorption rates
	17%	- NAS, 1976
Pulmonary		
Adult/child	40%	- See Table 3-1; reasonable approximation for inhalation of ambient air; no attempt has been made to allocate inhaled particles, based on size to pulmonary (<~3μm) or gastrointestinal (>~3μm) absorption routes
Dermal	insignificant	- Relatively unimportant, except in rare circumstances

to occur in episodes, possibly 2 to 3 times per week (NAS, 1976). It has been estimated that a child can consume somewhat greater than 1 gram within a 24-to 36-hour period, with cases reported of up to 20 grams within the same time period (Sachs, 1975) and that children with pica for paint may consume 1 to 3 grams per week (NAS, 1976). The low end of this range (1 g/wk) has been used in source contribution calculations as an estimate of paint intake in children with pica.

Pulmonary and gastrointestinal absorption rates utilized in subsequent calculations are also presented in Table 6-1. Most of these figures represent average absorption values for inhaled or ingested lead, as reported in the scientific literature. The absorption rate estimated for lead in soil/dust was intermediate between the absorption rates for lead in food and paint, since no value was found in the literature. Gastrointestinal absorption rates for children and adults are provided.

6.2 Estimated Daily Lead Uptake from All Sources

The relative contribution from each route of exposure (i.e., air, food, drinking water, soil/dust, paint) to an individual's total daily uptake has been determined from the specified environmental lead occurrence data (Table 6-2) in the calculation sequence described previously. Several concentrations of lead in drinking water have been utilized, along with representative ranges of lead in air, food, paint and soil/dust. Note that the values used represent average levels resulting from continuous, chronic exposure and do not reflect short term or episodic patterns of exposure (such as pica) which may be toxicologically significant. Table 6-2 provides those exposure values used in the calculations.

Dietary lead levels reflect daily lead intake excluding any contribution by beverages. In the studies cited (FDA, 1975), beverage intake for adults was less than half of the drinking water intake

TABLE 6-2

REPRESENTATIVE ENVIRONMENTAL LEAD EXPOSURE LEVELS

Exposure Routes		Remarks
Diet		
Adult (male)	208 µg/day	See Tables 2-4, 2-5; estimates based on reasonable range between diet preferences, excludes that contribution from beverages (including beverage contribution, 254 µg/day for adult, 115 for 3 yr. old child; adult female diet approximately 80% that of males)
(female)	166 µg/day	
Child (3 yr. old)	93 µg/day	
Ambient Air		
Urban average	0.89 µg/m^3	-See Table 2-1 for details; annual quarterly composite average NASN 1974 data
Non-Urban average	0.11 µg/m^3	
Ambient Air Standard	1.5 µg/m^3	-National ambient air quality standard (based on 90-day averaging)
Drinking Water	10 µg/l	
	25 µg/l	
	50 µg/l	-National interim primary drinking water standard
	100 µg/l	
Additional Exposure Routes for Children with Pica		
Paint	600 µg/g	-Current proposed standard
	8,000 µg/g	-Assumed mean, determined from existing house and market surveys (NAS, 1976; Bird, 1971)
Soil/dust (rural)	60 µg/g	Representative rural and urban values (Bethea and Bethea, 1975; Lepow et al., 1974; Rolfe and Haney, 1975)
(urban)	11,000 µg/g	

assumed in our calculations (0.9 and 2.0 l/day, respectively). The exclusion of beverage intake from the FDA estimates eliminated any double counting, since drinking water was entered in the calculations as a separate category. In addition, the lead concentrations in those beverages surveyed by the FDA were somewhat lower than the range of lead levels in water that were subsequently utilized, so any errors imparted by these manipulations would be toward conservatism.

Table 6-3 provides an example of the actual calculation sequence employed. The source contribution factors calculated for air, food and drinking water for the average adult male, based on the assumed sets of exposure conditions, are presented in Table 6-4. The factors for a pregnant female follow in Table 6-5.

Using the model for the lowest hypothetical urban exposure condition (lead in drinking water at 10 μg/l), representative intakes of 248 and 205 μg/day are indicated for the male and pregnant female, respectively. These values are in agreement with measured values (NAS, 1972; Goyer and Mushak, 1977; Tepper and Levin, 1975; Thompson, 1971; Goldberg, 1975). The source contribution factors for the average three-year-old child without pica and for the child with pica are given in Tables 6-6 and 6-7. The model indicates that urban exposure levels are much higher than has been reported by most studies. Those studies describing exposure conditions generally fail to include soil/dust levels, or underestimate the high concentrations of lead currently found in this exposure source (see Section 2.4). It should be noted that these tables represent presumed average values, and do not account for instances in which a particular environmental source is high. For example, ambient air lead concentrations averaged 0.89 $\mu g/m^3$ in 1974 (see Table 2-1), but the maximum reported quarterly composite was 4.09 $\mu g/m^3$. Obviously, in those instances the percent contribution from each source will shift to reflect these excursions.

TABLE 6-3

CALCULATION SEQUENCE IN DETERMINING SOURCE CONTRIBUTION FACTORS: CHILDHOOD CASE

SOURCE	CONCENTRATION	X	CONSUMPTION RATE	X	ABSORPTION RATE	=	DAILY UPTAKE IN CHILDREN	PERCENT OF TOTAL DAILY UPTAKE
Drinking water	50 μg/1		1.4 liters/day		0.50		35.0 μg/day	5.8
Air	1.5 $\mu g/m^3$		4.7 m^3/day		0.40		2.8 μg/day	<1
Food	93 μg/day		—		0.50		46.5 μg/day	7.7
Soil/dust	11,000 μg/g		100 mg/day		0.30		330.0 μg/day	54.3
Paint	8,000 μg/g		142 μg/day		0.17		193 μg/day	31.8
						Total	607.3 μg/day	

TABLE 6-4

ESTIMATED DAILY LEAD UPTAKE IN ADULT MALES (μg/day)

	RURAL				URBAN				AMBIENT AIR STANDARD			
	Source	Level	Uptake	Percent Contribution	Source	Level	Uptake	Percent Contribution	Source	Level	Uptake	Percent Contribution
Water @ 10 μg/1	Air	0.11 μg/m³	1.0	4.2	Air	0.89 μg/m³	8.1	26.2	Air	1.5 μg/m³	13.7	37.5
	Food	208 μg/day	20.8	87.4	Food	208 μg/day	20.8	67.3	Food	208 μg/day	20.8	57.0
	Drinking Water	10 μg/1	2	8.4	Drinking Water	10 μg/1	2	6.5	Drinking Water	10 μg/1	2.0	5.5
	Total		23.8		Total		30.9		Total		36.5	
Water @ 25 μg/1	Air	0.11 μg/m³	1.0	3.7	Air	0.89 μg/m³	8.1	23.9	Air	1.5 μg/m³	13.7	34.7
	Food	208 μg/day	20.8	77.6	Food	208 μg/day	20.8	61.4	Food	208 μg/day	20.8	52.6
	Drinking Water	25 μg/1	5.0	18.7	Drinking Water	25 μg/1	5.0	14.7	Drinking Water	25 μg/1	5.0	12.7
	Total		26.8		Total		33.9		Total		39.5	
Water @ 50 μg/1	Air	0.11 μg/m³	1.0	3.2	Air	0.89 μg/m³	8.1	20.8	Air	1.5 μg/m³	13.7	30.8
	Food	208 μg/day	20.8	65.4	Food	208 μg/day	20.8	53.5	Food	208 μg/day	20.8	46.7
	Drinking Water	50 μg/1	10.0	31.4	Drinking Water	50 μg/1	10.0	25.7	Drinking Water	50 μg/1	10.0	22.5
	Total		31.8		Total		38.9		Total		44.5	
Water @ 100 μg/1	Air	0.11 μg/m³	1.0	2.4	Air	0.89 μg/m³	8.1	16.6	Air	1.5 μg/m³	13.7	25.1
	Food	208 μg/day	20.8	49.8	Food	208 μg/day	20.8	42.5	Food	208 μg/day	20.8	38.2
	Drinking Water	100 μg/1	20.8	47.8	Drinking Water	100 μg/1	20.0	40.9	Drinking Water	100 μg/1	20.0	36.7
	Total		41.8		Total		48.9		Total		54.5	
Water @ 200 μg/1	Air	0.11 μg/m³	1.0	1.6	Air	0.89 μg/m³	8.1	11.8	Air	1.5 μg/m³	13.7	18.4
	Food	208 μg/day	20.8	33.7	Food	208 μg/day	20.8	30.2	Food	208 μg/day	20.8	27.9
	Drinking Water	200 μg/1	40.0	64.7	Drinking Water	200 μg/1	40.0	58.0	Drinking Water	200 μg/1	40.0	53.7
	Total		61.8		Total		68.9		Total		74.5	

TABLE 6-5

ESTIMATED DAILY LEAD UPTAKE IN PREGNANT FEMALES (µg/day)

	RURAL				URBAN				AMBIENT AIR STANDARD			
	Source	Level	Uptake	Percent Contribution	Source	Level	Uptake	Percent Contribution	Source	Level	Uptake	Percent Contribution
Water @ 10 µg/l	Air	0.11 $\mu g/m^3$	0.9	4.6	Air	0.89 $\mu g/m^3$	7.5	28.7	Air	1.5 $\mu g/m^3$	12.7	40.5
	Food	166 µg/day	16.6	85.1	Food	166 µg/day	16.6	63.6	Food	166 µg/day	16.6	53.1
	Drinking Water	10 µg/l	2.0	10.2	Drinking Water	10 µg/l	2.0	7.7	Drinking Water	10 µg/l	2.0	6.4
	Total		19.5		Total		26.1		Total		31.3	
Water @ 25 µg/l	Air	0.11 $\mu g/m^3$	0.9	4.0	Air	0.89 $\mu g/m^3$	7.5	25.8	Air	1.5 $\mu g/m^3$	12.7	37.0
	Food	166 µg/day	16.6	73.8	Food	166 µg/day	16.6	57.0	Food	166 µg/day	16.6	48.4
	Drinking Water	25 µg/l	5.0	22.2	Drinking Water	20 µg/l	5.0	17.2	Drinking Water	25 µg/l	5.0	14.6
	Total		22.5		Total		29.1		Total		34.3	
Water @ 50 µg/l	Air	0.11 $\mu g/m^3$	0.9	3.3	Air	0.89 $\mu g/m^3$	7.5	22.0	Air	1.5 $\mu g/m^3$	12.7	32.2
	Food	166 µg/day	16.6	60.4	Food	166 µg/day	16.6	48.7	Food	166 µg/day	16.6	42.3
	Drinking Water	50 µg/l	10.0	36.3	Drinking Water	50 µg/l	10.0	29.3	Drinking Water	50 µg/l	10.0	25.5
	Total		27.5		Total		34.1		Total		39.3	
Water @ 100 µg/l	Air	0.11 $\mu g/m^3$	0.9	2.4	Air	0.89 $\mu g/m^3$	7.5	17.0	Air	1.5 $\mu g/m^3$	12.7	25.7
	Food	166 µg/day	16.6	44.3	Food	166 µg/day	16.6	37.6	Food	166 µg/day	16.6	33.7
	Drinking Water	100 µg/l	20.0	53.3	Drinking Water	100 µg/l	20.0	45.4	Drinking Water	100 µg/l	20.0	40.6
	Total		37.5		Total		44.1		Total		49.3	
Water @ 200 µg/l	Air	0.11 $\mu g/m^3$	0.9	1.6	Air	0.89 $\mu g/m^3$	7.5	11.7	Air	1.5 $\mu g/m^3$	12.7	18.3
	Food	166 µg/day	16.6	28.9	Food	166 µg/day	16.6	25.9	Food	166 µg/day	16.6	24.0
	Drinking Water	200 µg/l	40.0	69.5	Drinking Water	200 µg/l	40.0	62.4	Drinking Water	200 µg/l	40.0	57.7
	Total		57.5		Total		64.1		Total		69.3	

TABLE 6-6

ESTIMATED DAILY LEAD UPTAKE IN CHILDREN WITHOUT PICA (μg/day)

	RURAL				URBAN				AMBIENT AIR STANDARD			
	Source	Level	Uptake	Percent Contribution	Source	Level	Uptake	Percent Contribution	Source	Level	Uptake	Percent Contribution
Water @ 10 μg/l	Air	0.11 μg/m³	0.2	<1	Air	0.89 μg/m³	1.7	<1	Air	1.5 μg/m³	2.8	<1
	Food	93 μg/day	46.5	83.8	Food	93 μg/day	46.5	12.1	Food	93 μg/day	46.5	12.0
	Soil/ Dust	60 μg/g	1.8	3.2	Soil/ Dust	11000 μg/g	330	85.7	Soil/ Dust	11000 μg/g	330	85.4
	Drinking Water	10 μg/l	7	12.6	Drinking Water	10 μg/l	7	1.8	Drinking Water	10 μg/l	7	1.8
	Total		55.5		Total		385.2		Total		386.3	
Water @ 25 μg/l	Air	0.11 μg/m³	0.2	<1	Air	0.89 μg/m³	1.7	<1	Air	1.5 μg/m³	2.8	<1
	Food	93 μg/day	46.5	70.5	Food	93 μg/day	46.5	11.8	Food	93 μg/day	46.5	11.7
	Soil/ Dust	60 μg/g	1.8	2.7	Soil/ Dust	11000 μg/g	330	83.4	Soil/ Dust	11000 μg/g	330	83.2
	Drinking Water	25 μg/l	17.5	26.5	Drinking Water	25 μg/l	17.5	4.4	Drinking Water	25 μg/l	17.5	4.4
	Total		66.0		Total		395.7		Total		396.8	
Water @ 50 μg/l	Air	0.11 μg/m³	0.2	<1	Air	0.89 μg/m³	1.7	<1	Air	1.5 μg/m³	2.8	<1
	Food	93 μg/day	46.5	55.7	Food	93 μg/day	46.5	11.3	Food	93 μg/day	46.5	11.2
	Soil/ Dust	60 μg/g	1.8	2.2	Soil/ Dust	11000 μg/g	330	79.9	Soil/ Dust	11000 μg/g	330	79.7
	Drinking Water	50 μg/l	35	41.9	Drinking Water	50 μg/l	35	8.5	Drinking Water	50 μg/l	35	8.4
	Total		83.5		Total		413.2		Total		414.3	
Water @ 100 μg/l	Air	0.11 μg/m³	0.2	<1	Air	0.89 μg/m³	1.7	<1	Air	1.5 μg/m³	2.8	<1
	Food	93 μg/day	46.5	39.2	Food	93 μg/day	46.5	10.4	Food	93 μg/day	46.5	10.3
	Soil/ Dust	60 μg/g	1.8	1.5	Soil/ Dust	11000 μg/g	330	73.6	Soil/ Dust	11000 μg/g	330	73.4
	Drinking Water	100 μg/l	70	59	Drinking Water	100 μg/l	70	15.6	Drinking Water	100 μg/l	70	15.6
	Total		118.5		Total		448.2		Total		449.3	
Water @ 200 μg/l	Air	0.11 μg/m³	0.2	<1	Air	0.79 μg/m³	1.7	<1	Air	1.5 μg/m³	2.8	<1
	Food	93 μg/day	46.5	24.6	Food	93 μg/day	46.5	9.0	Food	93 μg/day	46.5	9.0
	Soil/ Dust	60 μg/g	1.8	1.0	Soil/ Dust	11000 μg/g	330	63.7	Soil/ Dust	11000 μg/g	330	63.5
	Drinking Water	200 μg/l	140	74.2	Drinking Water	200 μg/l	140	27.0	Drinking Water	200 μg/l	140	27.0
	Total		188.5		Total		518.2		Total		519.3	

TABL

ESTIMATED DAILY LEAD UPTAKE IN

			RURAL						
	Source	Level	Uptake	Percent Contribution	Uptake	Percent Contribution	Source	Level	Upt
			Paint @ 600 μg/g		Paint @ 8000 μg/g				Paint @
Water @ 10 μg/l	Air	0.11 $\mu g/m^3$	0.2	<1	0.2	<1	Air	0.89 $\mu g/m^3$	1.7
	Food	93 μg/day	46.5	66.4	46.5	18.6	Food	93 μg/day	46.5
	Soil/Dust	60 μg/g	1.8	2.5	1.8	<1	Soil/Dust	11000 μg/g	330
	Paint		14.6	20.8	194.3	77.7	Paint		14.6
	Drinking Water	10 μg/l	7	10.0	7	2.8	Drinking Water	10 μg/l	7
	Total		70.1		249.8		Total		399.8
Water @ 25 μg/l	Air	0.11 $\mu g/m^3$	0.2	<1	0.2	<1	Air	0.89 $\mu g/m^3$	1.7
	Food	93 μg/day	46.5	57.6	46.5	17.9	Food	93 μg/day	46.5
	Soil/Dust	60 μg/g	1.8	2.2	1.8	<1	Soil/Dust	11000 μg/g	330
	Paint		14.6	18.1	194.3	74.6	Paint		14.6
	Drinking Water	25 μg/l	17.5	21.7	17.5	6.7	Drinking Water	25 μg/l	17.5
	Total		80.6		260.3		Total		410.3
Water @ 50 μg/l	Air	0.11 $\mu g/m^3$	0.2	<1	0.2	<1	Air	0.89 $\mu g/m^3$	1.7
	Food	93 μg/day	46.5	17.4	46.5	16.7	Food	93 μg/day	46.5
	Soil/Dust	60 μg/g	1.8	1.8	1.8	<1	Soil/Dust	11000 μg/g	330
	Paint		14.6	14.8	194.3	69.9	Paint		14.6
	Drinking Water	50 μg/l	35.0	35.6	35.0	12.6	Drinking Water	50 μg/l	35.0
	Total		98.1		277.8		Total		427.8
Water @ 100 μg/l	Air	0.11 $\mu g/m^3$	0.2	<1	0.2	<1	Air	0.89 $\mu g/m^3$	1.7
	Food	93 μg/day	46.5	34.9	46.5	14.8	Food	93 μg/day	46.5
	Soil/Dust	60 μg/g	1.8	1.4	1.8	<1	Soil/Dust	11000 μg/g	330
	Paint		14.6	10.9	194.3	62.1	Paint		14.6
	Drinking Water	100 μg/l	70.0	52.6	70.0	22.4	Drinking Water	100 μg/l	70.0
	Total		133.1		312.8		Total		462.8
Water @ 200 μg/l	Air	0.11 $\mu g/m^3$	0.2	<1	0.2	<1	Air	0.89 $\mu g/m^3$	1.7
	Food	93 μg/day	46.5	22.9	46.5	12.1	Food	93 μg/day	46.5
	Soil/Dust	60 μg/g	1.8	1	1.8	<1	Soil/Dust	11000 μg/g	330
	Paint		14.6	7.2	194.3	50.8	Paint		14.6
	Drinking Water	200 μg/l	140	68.9	140	36.6	Drinking Water	200 μg/l	140
	Total		203.1		382.8		Total		532.8

TABLE 6-7

IMATED DAILY LEAD UPTAKE IN CHILDREN WITH PICA FOR PAINT (µg/day)

URBAN

	Level	Uptake	Percent Contribution	Uptake	Percent Contribution
		Paint @ 600 µg/g		Paint @ 8000 µg/g	
	0.89 µg/m^3	1.7	<1	1.7	<1
	93 µg/day	46.5	11.6	46.5	8.0
ust	11000 µg/g	330	82.5	330	56.9
		14.6	3.7	194.3	33.5
ng					
r	10 µg/l	7	1.8	7	1.2
		399.8		579.5	
	0.89 µg/m^3	1.7	<1	1.7	<1
	93 µg/day	46.5	11.3	46.5	7.9
ust	11000 µg/g	330	80.4	330	55.9
		14.6	3.6	194.3	32.9
ng					
r	25 µg/l	17.5	4.3	17.5	3.0
		410.3		590.0	
	0.89 µg/m^3	1.7	<1	1.7	<1
	93 µg/day	46.5	10.9	46.5	7.7
ust	11000 µg/g	330	77.1	330	54.3
		14.6	3.4	194.3	32.0
ng					
r	50 µg/l	35.0	8.2	35.0	5.8
		427.8		607.5	
	0.89 µg/m^3	1.7	<1	1.7	<1
	93 µg/day	46.5	10.0	46.5	7.2
ust	11000 µg/g	330	71.3	330	51.4
		14.6	3.2	194.3	30.2
ng					
r	100 µg/l	70.0	15.1	70.0	10.9
		462.8		642.5	
	0.89 µg/m^3	1.7	<1	1.7	<1
	93 µg/day	46.5	8.7	46.5	6.5
ust	11000 µg/g	330	61.9	330	46.3
		14.6	2.7	194.3	27.3
ng					
r	200 µg/l	140	26.3	140	19.6
		532.8		712.5	

AMBIENT AIR STANDARD

Source	Level	Uptake	Percent Contribution	Uptake	Percent Contribution
		Paint @ 600 µg/g		Paint @ 8000 µg/g	
Air	1.5 µg/m^3	2.8	<1	2.8	<1
Food	93 µg/day	46.5	11.6	46.5	8.0
Soil/Dust	11000 µg/g	330	82.3	330	56.8
Paint		14.6	3.6	194.3	33.5
Drinking Water	10 µg/l	7.0	1.7	7.0	1.2
Total		400.9		580.6	
Air	1.5 µg/m^3	2.8	<1	2.8	<1
Food	93 µg/day	46.5	11.3	46.5	7.9
Soil/Dust	11000 µg/g	330	80.2	330	55.8
Paint		14.6	3.5	194.3	32.9
Drinking Water	25 µg/l	17.5	4.3	17.5	3.0
Total		411.4		591.1	
Air	1.5 µg/m^3	2.8	<1	2.8	<1
Food	93 µg/day	46.5	10.8	46.5	7.6
Soil/Dust	11000 µg/g	330	76.9	330	54.2
Paint		14.6	3.4	194.3	31.9
Drinking Water	50 µg/l	35.0	8.2	35.0	5.8
Total		428.9		608.6	
Air	1.5 µg/m^3	2.8	<1	2.8	<1
Food	93 µg/day	46.5	10.0	46.5	7.2
Soil/Dust	11000 µg/g	330	71.1	330	51.3
Paint		14.6	3.1	194.3	30.2
Drinking Water	100 µg/l	70.0	15.1	70.0	10.9
Total		463.9		643.6	
Air	1.5 µg/m^3	2.8	<1	2.8	<1
Food	93 µg/day	46.5	8.7	46.5	6.5
Soil/Dust	11000 µg/g	330	61.8	330	46.2
Paint		14.6	2.7	194.3	27.2
Drinking Water	200 µg/l	140	26.2	140	19.6
Total		533.9		713.6	

TABLE 6-7
ESTIMATED DAILY LEAD UPTAKE IN CHILDREN WITH PICA FOR PAINT (µg/day)

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The range of calculated source contribution factors is quite large, if one considers all the possible permutations of lead levels specified for the various media. In adults, the source contribution factor for drinking water varies from about 5 to 70 percent. In children without pica, drinking water contributes between 2 and 74 percent of the daily lead uptake. For the child with pica for paint, drinking water contributes between 1 and 37 percent, depending on the concentration of lead in soil/dust and paint. In a child with pica for paint, soil/dust can account for as much as 82 percent of the daily lead uptake, while paint can contribute as much as 78 percent. The contribution from air varies from about 2 to 41 percent for an adult and is almost insignificant for a child. Ambient lead levels in air can be significantly higher than the values presented in Tables 6-4 through 6-7, so the assumed range in atmospheric concentrations is somewhat restricted. The contribution of food to an individual's total daily lead uptake varies from 24 to 87 percent for an adult, from 9 to 84 percent for a child without pica, and from 7 to 66 percent for a child with pica for paint. The total daily lead uptake in children is always higher than that predicted for adults.

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7.0 LEAD-UPTAKE/BLOOD-LEAD RELATIONSHIPS

Blood lead is the most widely used indicator of recent lead exposure. It is also regarded as a reasonable surrogate for the biological response associated with lead absorption. Since this is the value most often reported in the literature to represent the extent of lead absorption, it is necessary to relate daily lead uptake to blood-lead values in order to define the toxicological impact associated with the different levels of lead uptake determined by the source contribution model. Because children and fetuses have been identified as sensitive populations, it is necessary to derive this lead-uptake-to-blood-lead relationship for both children and pregnant women.

7.1 Child Relationship

There are no comprehensive studies in the literature which report a lead-uptake-to-blood-lead relationship for children. Although there are studies for adults, these can not be used to define a relationship for children due to the differences in exposure conditions and metabolic differences. Therefore, it has been necessary to derive a relationship from the combined data of a number of studies.

Data from six epidemiological studies have been used to derive a relationship between lead-uptake and blood-lead values for children. These studies were selected because each specified an environmental lead level for most of the major sources of exposure, gave the levels for different exposure conditions (i.e., high and low exposure levels) and reported corresponding blood-lead levels for each exposure circumstance.

Table 7-1 provides the data from these six studies. Since not all of the studies had values for every environmental source, it was necessary to assume values in such cases. Footnotes in the table

TABLE 7-1

ENVIRONMENTAL LEAD CONCENTRATION AND BLOOD LEAD IN CHILDREN: SELECTED SITES[a]

	ENVIRONMENTAL LEAD CONCENTRATION					LEAD UPTAKE		BLOOD LEAD
	Food (μg/day)	Drinking Water (μg/l)	Air (μg/m^3)	Soil/Dust[b] (μg/g)	Paint[c] (μg/g)	Total (μg/kg/day)	Via Ingestion (μg/kg/day)	Reported (μg/dl)
Toronto (Roberts et al., 1974)	93[d]	6.8	3.84	3503	12300	30.8	30.3	31
	93[d]	1.4	0.93	652	13000	25.6	25.5	19
El Paso (Landrigan et al., 1975; Angle and McIntire, 1978)	93[d]	50[e]	4.4	2005	10000	26.2	25.6	31.2
	93[d]	50[e]	1.3	953	10000	23.7	23.5	20.1
Shoshone/Silver Valley (Idaho Dept. of Health and Welfare, 1977)	93[d]	50	16.8	8516.7	10340	45.3	39.2	68.3
	93[d]	50	14.2	8055.7	13139	44.5	42.8	49.1
	93[d]	50	6.6	1739.7[f]	3847.9	16.0	15.1	34.7
	93[d]	50	3.0	3256.4	9588.2	27.8	27.5	33.3
	93[d]	50	0.7	2800.2	16503.3	37.8	37.8	28.8
	93[d]	50	0.5	1042.3[f]	15017.8	31.9	31.8	21.9
	93[d]	50	0.5	2295.2	10264.2	26.7	26.6	31.0
Bennington (CDC, 1978)	93[d]	13.7	0.7[g]	670[h]	8000[j]	18.1	18.0	14.7
	93[d]				600[k]	6.1	6.1	14.7
	93[d]	66	0.7[g]	670[h]	8000[j]	20.6	20.5	16.4
	93[d]				600[k]	8.6	8.5	16.4
	93[d]	51	0.7[g]	670[h]	8000[j]	19.8	19.8	18.2
	93[d]				600[k]	7.9	7.8	18.2

TABLE 7-1 (CONCLUDED)

	ENVIRONMENTAL LEAD CONCENTRATION					LEAD UPTAKE		BLOOD LEAD
	Food (μg/day)	Drinking Water (μg/1)	Air (μg/m^3)	Soil/Dust[b] (μg/g)	Paint[c] (μg/g)	Total (μg/kg/day)	Via Ingestion (μg/kg/day)	Reported (μg/dl)
Los Angeles (Johnson et al., 1975[a])	93[d]	50[e]	6.3	1000[fm]	8000[j]	21.2	20.4	20.1
	93[d]				600[k]	9.2	8.4	20.1
	93[d]	50[e]	0.64	66.8[f]	8000[j]	18.6	18.5	11.0
	93[d]				600[k]	6.6	6.5	11.0
Omaha (Angle and McIntire, 1978)	93[d]	0.1	0.7	375.7	8000[j]	16.9	16.8	25.6
	93[d]	0.1			600[k]	4.9	4.9	25.6
	93[d]	0.1	0.4	167.8	8000[j]	16.5	16.4	14.6
	93[d]	0.1			600[k]	4.5	4.4	14.6

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[a] All concentrations are arithmetic means.

[b] Average soil exterior dust, and interior dust values (unless otherwise noted).

[c] Represents indoor paint concentrations (exterior paint not considered).

[d] Assumed Pb ingestion via food = 93 μg/day.

[e] Assumed Pb in water = 50 μg/liter.

[f] Average soil concentration and interior dust concentration.

[g] From Preston, 1977.

[h] Represents average indoor dust value.

[j] High paint estimate = 8000 ppm (based on existing house and market surveys).

[k] Low paint estimate = 600 ppm (proposed new standard of 0.06 percent Pb concentration).

[m] Assumed mean from Angle and McIntire, 1978.

describe the values used. In determining the total lead absorbed, the absorption factors associated with the three-year-old, 15-kg child were used. These factors have been previously identified in Sections 3.0 and 6.0. Figure 7-1 shows the straight-line relationship ($y = 0.80x + 7.85$; $r = 0.73$) derived using data points based on these studies.

The relationship based on total uptake (Figure 7-1) appears to predict blood-lead values which agree with other reported values. For example, at the specified urban background levels for the child without pica (385.2 μg uptake/day; see Table 6-6), this relationship predicts a blood-lead level of 28.4 μg/dl. Other studies (Adebonojo, 1974; Joselow et al., 1975) place the estimate in the range of 28 to 30 μg/dl.

7.1.1 Comparison with Other Relationships

Since data from other studies relating absorbed lead to blood lead do so on the basis of ingested lead only, it was necessary to derive another relationship based on that portion of the daily uptake associated with ingested lead only. To do this, that portion of the total daily uptake which was derived from the contribution by air was subtracted, and the remainder (total uptake via ingestion) was equated with the reported blood-lead levels. The amount to be subtracted was determined by using the source contribution factors identified in Tables 6-1 and 6-2. The values for lead uptake via ingestion only were also provided in Table 7-1.

Several studies have described an ingested lead-to-blood-lead relationship for children. Two relationships which will be considered for comparison are those proposed by the National Academy of Sciences (1972) and by Moore et al. (1977).

Clinical studies involving adult volunteers have determined that the supplemental ingestion of 1 mg/day of lead as lead acetate or lead chloride produces a 17 μg/dl rise in blood-lead level over a period of several months (Kehoe, 1961). If one assumes a gastrointestinal absorption rate of 10 percent in adults, then the 1 mg/day

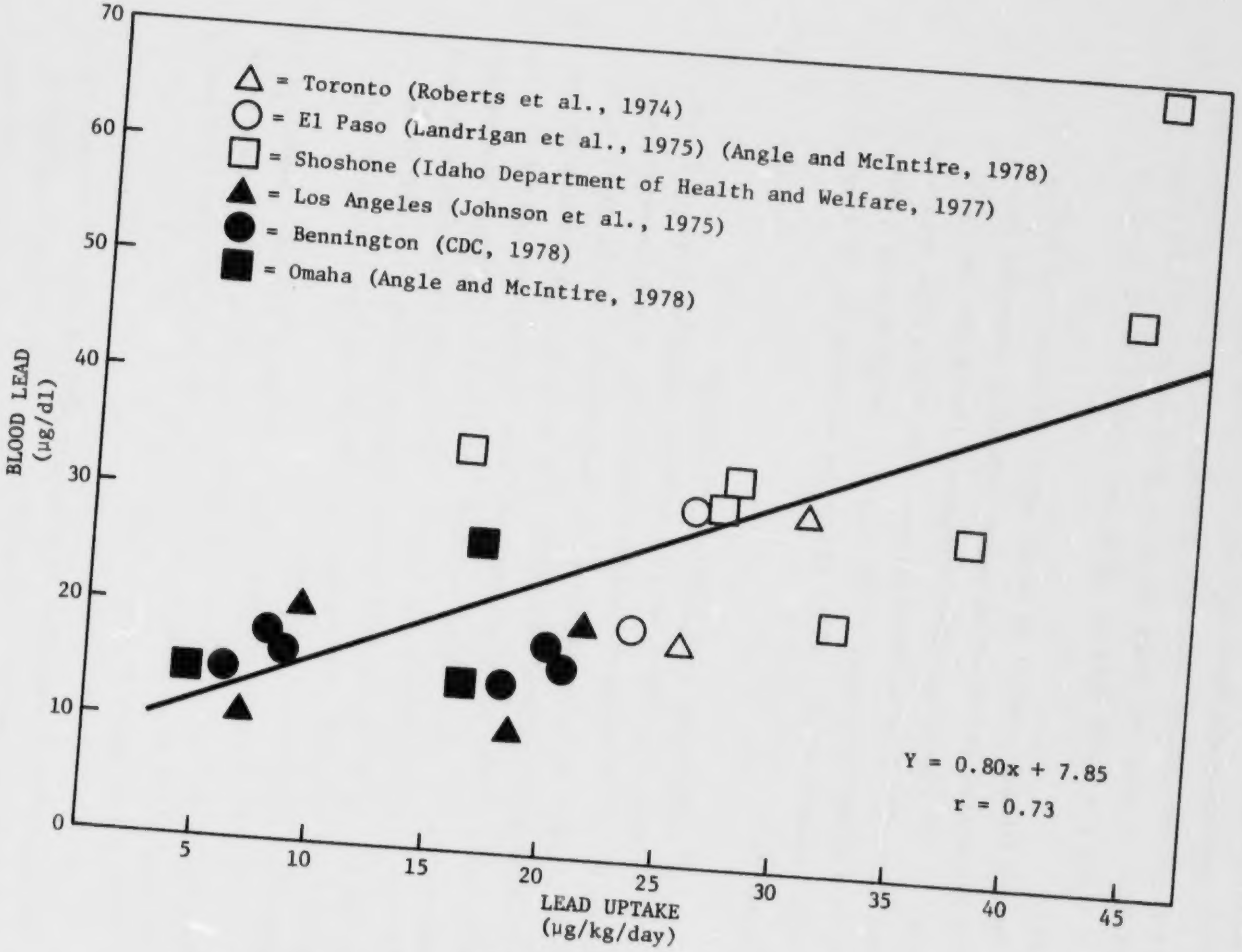


FIGURE 7-1
TOTAL DAILY ABSORBED LEAD TO BLOOD-LEAD RELATIONSHIP
FOR THE CHILD

intake rate corresponds to an uptake rate of 100 μg of lead per day. For the average (70 kg) adult, the lead absorbed daily to produce the 17 μg/dl rise in blood-lead levels would be about 1.43 μg Pb/kg/day. NAS (1976) assumed in developing their relationship that an increase in lead uptake of 1.43 μg/kg/day in children will also produce a 17 μg/dl rise in blood lead. Barltrop and Killala (1967) found that a group of two-to-three-year old children with a mean blood-lead level of 20 μg/dl excreted an average of 67.8 μg Pb/day/ person in the feces. Assuming that this fecal lead was the 50 percent of ingested lead that was not absorbed by the gastrointestinal tract, the daily uptake of ingested lead by the average (15 kg) child would be 4.5 μg/kg/day. The slope obtained from Kehoe (1961) data and these average lead uptake and blood-lead values were used by the NAS (1976) to specify a lead uptake-to-blood-lead relationship. It should be pointed out that the relationship considers only ingested lead and does not differentiate between lead in drinking water and lead in food.

The relationship proposed by Moore et al. (1977) is based on a study involving neonates (10 days postpartum) to determine if any association existed between blood-lead levels and mental retardation. This study was carried out in Scotland, where drinking water-lead levels were in excess of 100 μg/l. In this study, blood-lead levels were compared to water-lead concentrations in the maternal home during pregnancy (Moore et al., 1977). No attempt was made to account for other sources of lead exposure (i.e., air, soil/dust, paint), or to determine the actual quantities of lead in the drinking water ingested. This study does, however, provide an indication of the long-term impact of high lead levels in water on blood-lead levels of the indigenous population.

Figure 7-2 illustrates how these relationships compare with the relationship developed from the six epidemiological studies on the basis of ingested lead only. It was assumed that the blood-lead values reported in the NAS (1976) and Moore et al. (1977) studies were actual measured values. Since these values represent the contributions from both ingested and inhaled lead, the reported blood-lead values from the six epidemiological studies were used in deriving MITRE's ingested lead-only line. As can be seen in the figure, the slopes of the lines are different and the choice of curve will have a substantial effect on the value predicted for blood-lead concentration.

The relationship developed from the six studies (uptake via ingestion only) appears to agree well with the relationship derived from the Moore et al. (1977) study. However, since the data of the latter were obtained from ten-day-old infants, it is not certain how representative these data are, since the mother's blood-lead concentration (as previously described) will have a major influence on the child's blood-lead concentration at this early stage of life.

The NAS relationship predicts a much greater increase in blood-lead values than either of the other two relationships, with incremental increases in the amount of lead absorbed. This difference may be partially explained by the fact that the relationship was developed by extrapolating adult data to conform with the intake and absorption characteristics of a three-year-old child, thereby ignoring any other metabolic differences between adults and children.

7.1.2 Major Assumptions

Several assumptions are necessary when using this relationship. It is assumed that the relationship is approximately linear over a specific range of absorption values (about 4 to 50 μg/kg/day) and blood-lead values (i.e., 12 to 40 μg/dl). Other studies (Moore et al., 1977; Berlin et al., 1977; Goldberg, 1974) have suggested that the relationship may not be linear. It is further assumed that daily

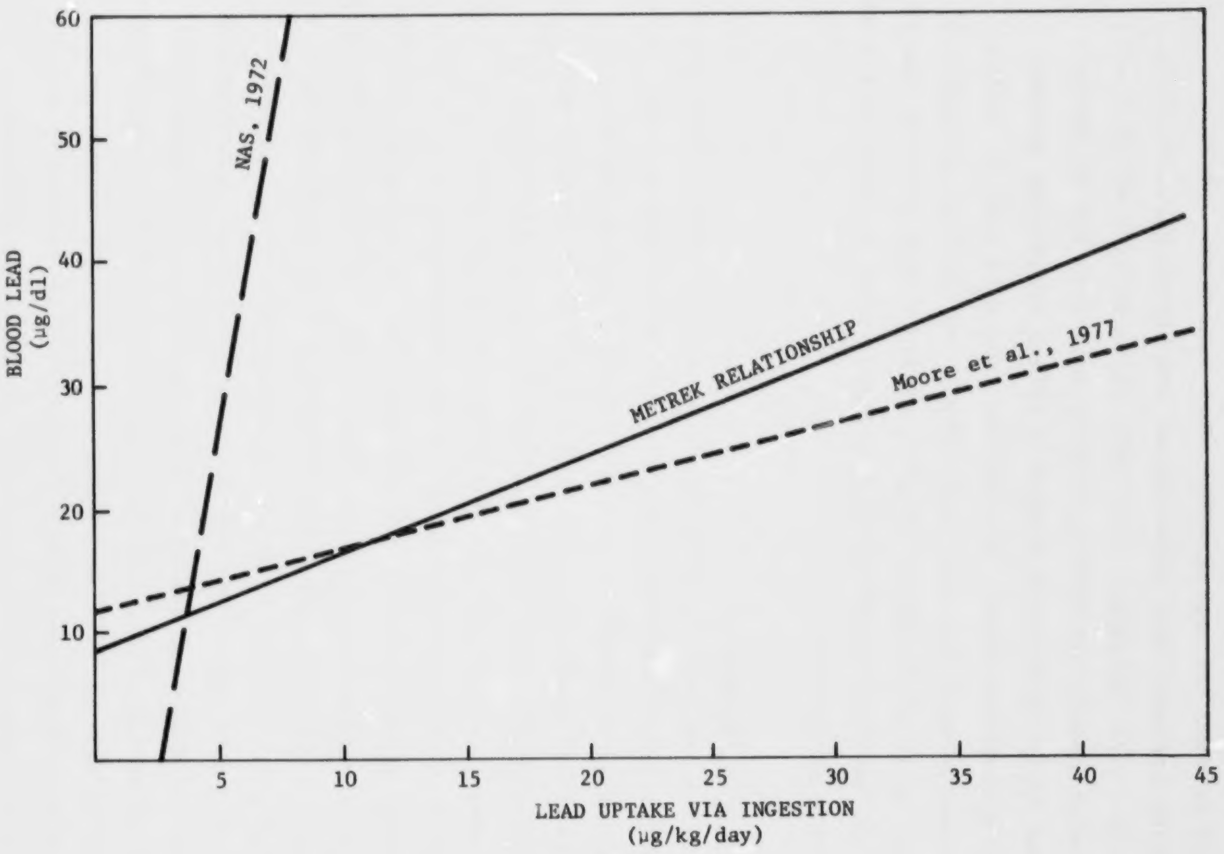


FIGURE 7-2
RELATIONSHIPS BETWEEN LEAD UPTAKE VIA INGESTION AND BLOOD LEAD FOR THE CHILD

intake values, as well as absorption rates for several environmental sources (i.e., food, soil/dust, paint) were fairly constant in the populations studied and approximated those used here. There are studies which indicate that these values are highly variable (King, 1971; Lin-Fu, 1972; Mahaffey, 1977; NAS, 1976; Roberts et al., 1974).

The relationship was developed using data from six different studies and applying the best available values concerning average intake and absorption rates. In addition, the data used to derive the relationship were specific to children. As has been pointed out previously, it is necessary to use data obtained from children due to exposure and metabolic differences. Extrapolation of adult data leads to inaccurate predictions.

7.2 Adult Relationship

The fetus has been identified as sensitive to lead. There is a close association between fetal and maternal blood-lead levels. Therefore, it is necessary to discuss the relationship between absorbed lead and blood lead for women. Although no studies were found which reported data relating absorbed lead to blood lead in pregnant women, several general statements concerning this relationship in adults can be found in the literature.

Clinical studies suggest a blood-lead rise of 1.7 μg/dl for every 100 μg of ingested lead (Kehoe, 1961). Data reviewed by Barltrop (1977) lead to the conclusion that blood-lead levels are increased by approximately 2 μg/dl for each 100 μg of ingested lead. Several investigators have correlated increases in water-lead concentrations with rises in blood-lead levels. These data have been compiled and presented by Berlin et al. (1977). Table 7-2 summarizes these data. These results were obtained for water concentrations around 100 μg/l. The mean from these values is a rise of approximately a 2.5 μg/dl in blood lead for every 100 μg/l increase in water-lead concentration.

TABLE 7-2

RISE IN BLOOD LEAD LEVEL ASSOCIATED WITH INCREASE OF 100 μg/l IN WATER LEAD CONCENTRATION

RISE IN BLOOD LEAD (μg/dl)	WATER LEAD SAMPLING PROTOCOL
1.3	Running Sample
1.2	First Flush
3.4	Running Sample
3.3	First Flush
1.8	---
2.0	Running Sample
6.0	Running Sample
3.9	First Flush
0.83	---
1.9	First Flush
5.3	Full Flush
0.72	First Flush
1.3	First Flush

SOURCE: Adapted from Berlin et al., 1977.

An additional study (EPA, 1977) suggested a range for the absorbed-lead-to-blood-lead relationship. This range was based on data from studies involving lead absorbed from food and water in adult populations. From these studies, it was estimated that for every 100 μg of ingested lead, a 6 to 18 μg/dl rise in blood lead would be expected. However, it is apparent that a relationship which assumes a rise in blood lead of approximately 2 μg/dl for every 100 μg of ingested lead more closely approximates the majority of values reported in the literature. Therefore, this relationship will be considered representative.

Mean blood-lead levels and corresponding estimated uptake values (through the source contribution model) were used as starting points for deriving a line to depict the adult absorbed-lead-to-blood-lead relationship. Reported values for average blood-lead levels in adults vary according to sex: female levels are lower than those of males. Three studies were used to define average blood-lead values for urban women. The three reported values were 13.8 μg/dl (based on 100 women [Goldsmith, 1974]), 13.8 μg/dl (based on 52 women [Johnson et al., 1975]), and 19.0 μg/dl (based on more than 400 women [Tepper and Levin, 1975]). An average of these values, about 15 μg/dl, was chosen as the representative blood-lead level for an urban woman.

Representative urban environmental lead levels were used to define the intake one would expect for an urban female. Using these levels (i.e., air @ 1.5 μg/m^3, food @ 166 μg/day, and water @ 10 μg/l), an intake of 200 μg would be expected. This level is well within the range reported by a number of authors (NAS, 1972; Goyer and Mushak, 1977; Tepper and Levin, 1975; Thompson, 1971; Goldberg, 1975; Mahaffey, 1977) and is considered representative.

Using the absorption values for adults, this intake would correspond to an uptake of 31.47 μg Pb/day. Thus, a blood-lead level of

15 μg/dl would be expected to result from an uptake of 31.47 μg Pb/day. Converting this to the μg/kg/day scale, assuming a body weight of 60 kg, would produce an uptake value of 0.524 μg/kg/day. Figure 7-3 shows the relationship derived when using these values. The line ($y = 14.1x + 7.67$) passes through the point defined as the mean urban blood-lead level/mean urban absorption level, and has a slope based on the relationship of a 2 μg/dl rise in blood lead for every 100 μg of ingested lead.

The ratio of 2 μg/dl rise in blood lead for every 100 μg of ingested lead was developed from data which reported a blood-lead range of up to about 30 to 35 μg/dl. For this reason, the relationship is believed to be approximately linear up to this level. In at least one study of blood-lead levels associated with high drinking-water-lead levels (Goldberg, 1975), it was suggested that a curvilinear relationship may be more representative at even lower blood-lead levels. However, until further data are produced, it will be assumed that the linear relationship is adequate for the ranges reported here.

This relationship can be used to predict blood-lead levels for the female, pregnant female, and adult male since the scale allows for differing body weights. In addition, this relationship appears valid for the pulmonary intake route. EPA (1977) reports a ratio of rise in blood-lead levels to increase in ambient air lead concentrations of 2 μg/dl blood lead per 1 $\mu g/m^3$ air lead. Assuming an increase in air lead concentration of 1 $\mu g/m^3$, an average adult male would inhale 22.8 μg Pb/day, while an average adult female would inhale 21.1 μg/day. At a pulmonary absorption rate of 40 percent, the increase in uptake for the male would be 9.12 μg/day and the for the female, 8.44 μg/day. These increases in uptake correspond to increases in blood-lead levels of 1.8 μg/dl in the male and 1.7 μg/dl in the female. This compares favorably with the EPA prediction of a 2 μg/dl blood-lead increase for an increase of 1 μg/m3 in air lead.

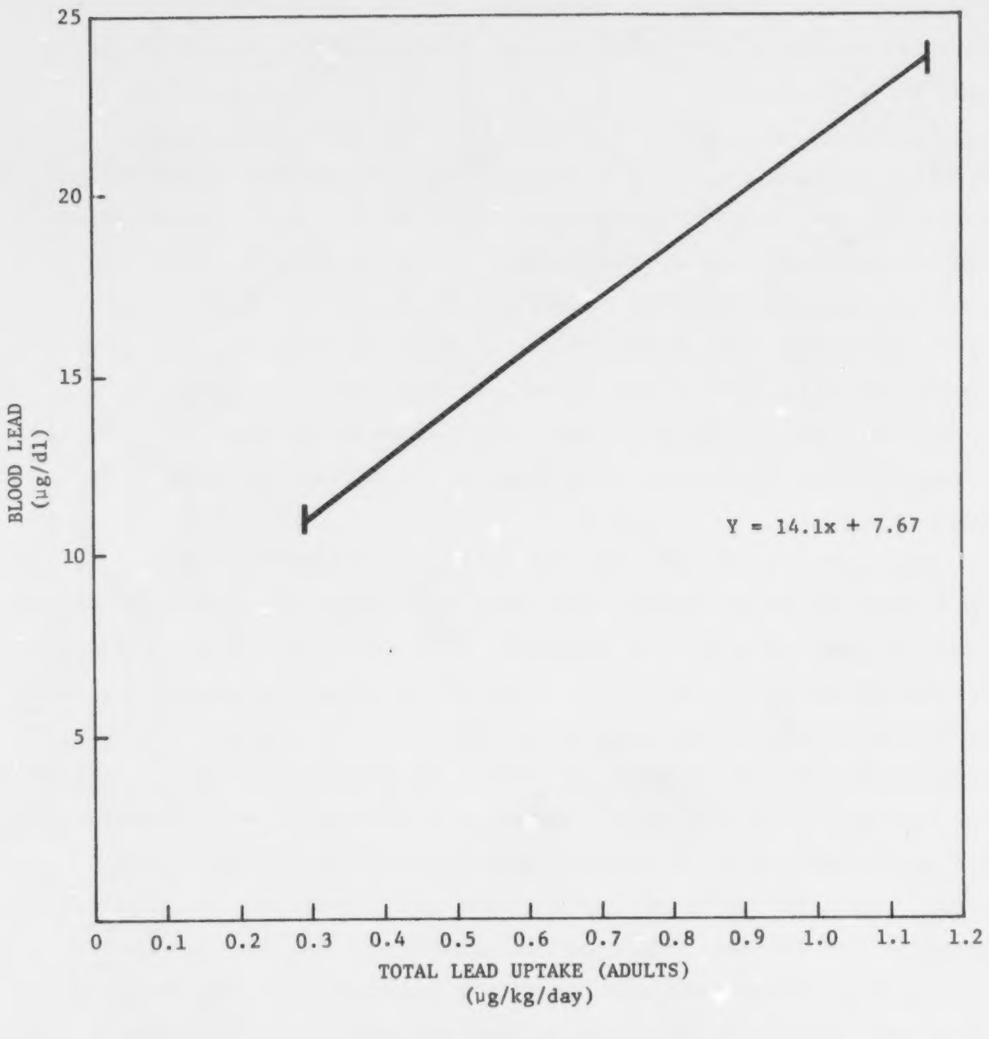


FIGURE 7-3
TOTAL DAILY ABSORBED LEAD TO BLOOD-LEAD
RELATIONSHIP FOR THE FEMALE ADULT

Thus, using this relationship, one can determine the estimated rise in blood lead which would be expected in an adult following an increase in the amount of lead absorbed from any environmental source, including drinking water.

7.3 Comparison of the Relationships

None of the epidemiological or clinical studies reviewed by MITRE has unequivocally characterized the physiological basis or mathematical form of the lead-uptake-to-blood-lead relationship in either children or adults. Although many of these studies have concluded that the relationships are adequately represented by linear functions, a number of authors have suggested that the relationships are nonlinear.

The straight-line, lead-uptake-to-blood-lead relationships utilized by Metrek are based on data reporting lead intake levels and corresponding blood-lead levels and are presumed to have no more physiological significance than that which is evidenced by their conformity to these data. Linear functions were selected because: (1) they appeared to adequately approximate experimental results (2) there was no overwhelming evidence to suggest that the relationship is nonlinear and no clearcut characterization of the form of such a relationship; and (3) they were simple to derive and manipulate. Since the equations have limited physiological significance, there is little or no justification for using them to extrapolate blood-lead values associated with uptake levels that are very far beyond the range of the available data or beyond the normal uptake ranges defined by the source contribution model (approximately 3 to 50 μg/kg/day for children and 0.3 to 1.2 μg/kg/day for adults).

The relationships developed by MITRE predict that an incremental increase in lead uptake will produce a greater increase in blood lead in a pregnant woman than in a young child. However, since the two relationships are presumed to be valid only within specific, nonoverlapping uptake ranges this observation does not necessarily signify physiological differences, other than in uptake rates, between children and pregnant females. A single nonlinear function could conceivably describe the actual lead-uptake-to-blood-lead relationship for both populations and would produce the observed results. However, it is likely that physiological differences are at least partially responsible for the observed difference in the slope of the relationships. Children may more readily accept lead into their relatively empty dense bone pool than adults, and thus retain a smaller fraction in the blood and tissues which exchange rapidly with it. Even if there were actual physiological differences resulting in two, more-or-less similar curves, these differences would not be apparent from the available data. The regions of the curves in closest proximity to each other represent extremely high lead intake levels for adults and extremely low intake levels for children; therefore, corresponding portions of the two curves would never be manifested in a single population.

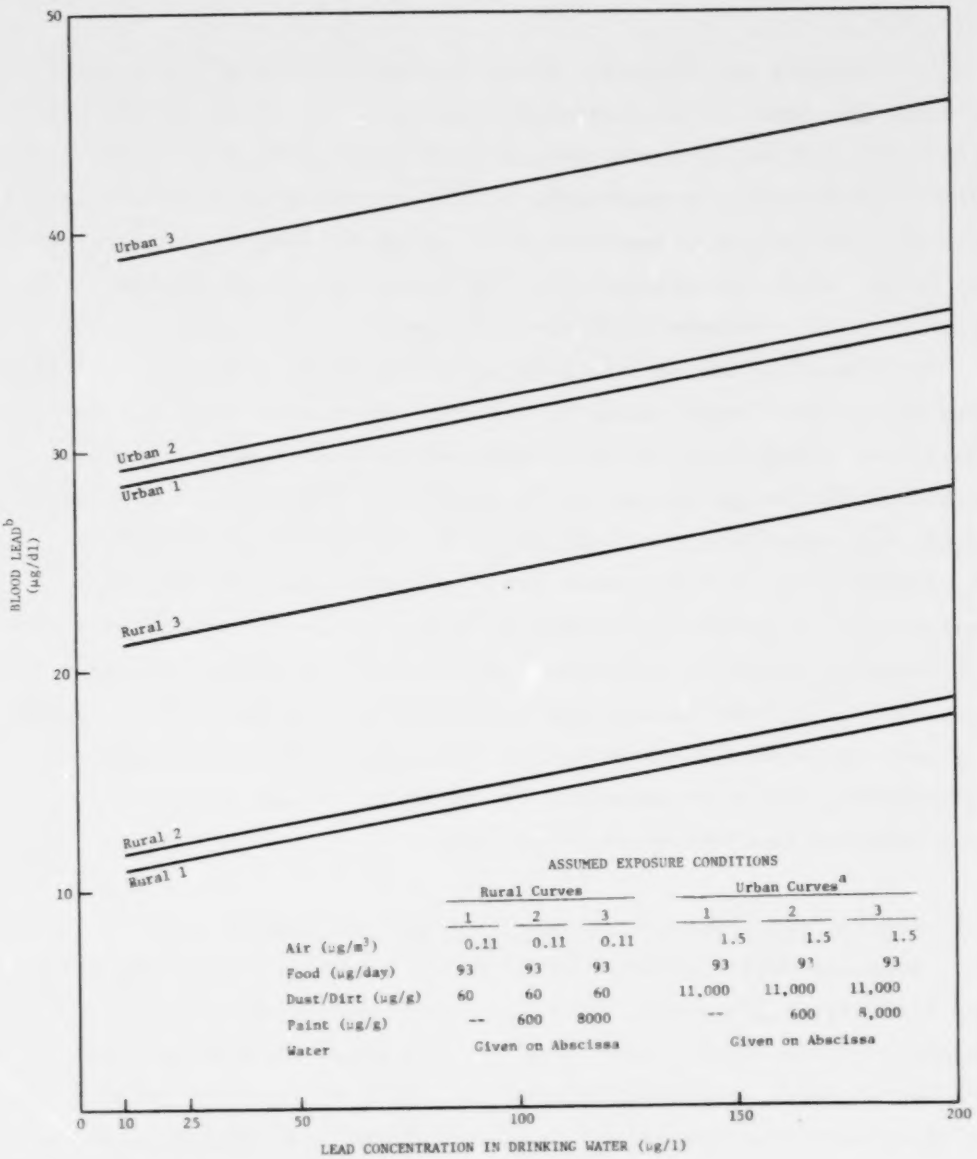
8.0 WATER-LEAD/BLOOD-LEAD SCENARIOS

To evaluate the adequacy of the interim primary drinking water standard for lead, it is necessary to predict the blood-lead levels associated with various concentrations of lead in drinking water for identified sensitive populations, and to determine the extent to which altering the maximum allowable concentration of lead in drinking water may affect these populations (via the toxicological consequences associated with changes in blood-lead levels).

By combining the derived lead-uptake-to-blood-lead relationship with the percent contribution values from the source contribution model, the relationship between varied water-lead exposure and resultant blood-lead values can be drawn. In the source contribution model, any specific subunit of the total population is defined by representing the characteristic exposure concentrations and physiologic parameters associated with that subunit. Furthermore, the considerable variation from predicted average exposure levels seen in some subunits of the population, particularly children, and in certain regional or local situations (e.g., close proximity to smelting operations), can be accommodated by the model, since any set of environmental conditions can be utilized.

8.1 Water-Lead-to-Blood-Lead Relationship in Children

Separate water-lead-to-blood-lead relationships have been defined for the following specific subunits of the child population: rural children without pica, rural children with pica for paint who are exposed to paint containing lead at the current standard, rural children with pica exposed to paint containing lead at levels above the standard, and urban children in the same three categories (Figure 8-1). The assumed exposure conditions are given on the figure; the



ASSUMED EXPOSURE CONDITIONS

	Rural Curves			Urban Curves[a]		
	1	2	3	1	2	3
Air ($\mu g/m^3$)	0.11	0.11	0.11	1.5	1.5	1.5
Food (µg/day)	93	93	93	93	93	93
Dust/Dirt (µg/g)	60	60	60	11,000	11,000	11,000
Paint (µg/g)	--	600	8000	--	600	8,000
Water	Given on Abscissa			Given on Abscissa		

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[a] Air at ambient standard.

[b] Blood-lead levels calculated from total uptake, based on exposure conditions shown.

FIGURE 8-1
EFFECTS OF VARYING LEAD CONCENTRATIONS IN DRINKING WATER ON THE BLOOD-LEAD LEVELS OF A HYPOTHETICAL 2 YEAR OLD CHILD

lead concentrations in drinking water is given on the abscissa. The six resultant relationships allow comparison of the effect on blood lead of increasing water-lead concentrations in urban and rural children.

The relationships between water-lead exposure and blood-lead levels (Figure 8-1) share a common slope since each reflects the same rate of change in total uptake. Therefore, each shows the same constant increase in blood lead over the range of water lead considered. The total blood-lead increase over the range of 10 to 200 μg/l lead in water is 6.7 μg/dl, represented as a slope of 0.035 in each of the lines in Figure 8-1. The y-intercept of each line has been determined by calculating the total lead uptake from all sources except water and then calculating the expected blood lead at this uptake.

Analysis of the effect of varied water-lead intakes in reference to the critical threshold level of 30 μg/dl, chosen by EPA and CDC, reveals urban children as the sensitive subgroup. Although water may comprise as much as 42 percent of the source contribution in rural children exposed to lead in drinking water at the current standard, their total blood lead (12.3 μg/dl) is well below the critical threshold level (see Table 8-1). Urban children without pica, at the current drinking water standard and above, have blood-lead values near the critical threshold level. Urban children with pica for paint (with lead-containing paint at the current standard) have blood-lead levels of 30 μg/dl at water-lead levels below the current standard (50 μg/l), and blood-lead values well above the critical threshold level at water-lead levels above the standard. Urban children with pica (with lead-containing paint above the standard) display blood-lead levels well above the critical level at water-lead levels below the current standard (Table 8-2).

TABLE 8-1

ESTIMATED DAILY LEAD UPTAKE AND BLOOD LEAD IN CHILDREN WITHOUT PICA

	RURAL		URBAN		AMBIENT AIR STANDARD	
[Pb] in Water	Total Daily Uptake (μg)*	Blood Lead μg/dl	Total Daily Uptake (μg)*	Blood Lead μg/dl	Total Daily Uptake (μg)*	Blood Lead μg/dl
10 μg/l	55.5	10.8	385.2	28.4	386.3	28.5
25 μg/l	66.0	11.4	395.7	29.0	396.8	29.0
50 μg/l	83.5	12.3	413.2	29.9	414.3	29.9
100 μg/l	118.5	14.2	448.2	31.8	449.3	31.8
200 μg/l	188.5	17.9	518.2	35.5	519.3	35.5

*See Table 6-6 for source contributions to total daily uptake

TABLE 8-2

ESTIMATED DAILY LEAD UPTAKE AND BLOOD LEAD IN CHILDREN WITH PICA FOR PAINT

		RURAL		URBAN		AMBIENT AIR STANDARD	
[Pb] in Water	[Pb] in Paint	Total Daily Uptake (μg)*	Blood Lead (μg/dl)	Total Daily Uptake (μg)*	Blood Lead (μg/dl)	Total Daily Uptake (μg)*	Blood Lead (μg/dl)
10 μg/1	600	70.1	11.6	399.8	29.2	400.9	29.2
	8000	249.8	21.2	579.5	38.8	580.6	38.8
25 μg/1	600	80.6	12.1	410.3	29.7	411.4	29.8
	8000	260.3	21.7	590.0	39.3	591.1	39.4
50 μg/1	600	98.1	13.1	427.8	30.7	428.9	30.7
	8000	277.8	22.7	607.5	40.3	608.6	40.3
100 μg/1	600	133.1	14.9	462.8	32.5	463.9	32.6
	8000	312.8	24.5	642.5	42.1	643.6	42.2
200 μg/1	600	203.1	18.7	532.8	36.3	533.9	36.3
	8000	382.8	28.3	712.5	45.9	713.6	45.9

*See Table 6-7 for source contributions to total daily uptake

At the current water standard, water lead represents 8.5 and 8.2 percent of the total source contribution for urban children without pica and urban children with pica for paint (lead-containing paint at the standard), respectively. In children with pica, with lead-containing paint above the standard (8000 μg/g), water lead provides 5.8 percent of the total daily lead uptake. Thus it is evident that water contributes only a small amount to the blood-lead level of children compared to other environmental exposures (i.e., soil/dust and paint). In pica children (paint lead at 8000 μg/g) lowering the water-lead concentration from 50 to 10 μg/l produces a decrease in the percent contribution of water lead to total daily lead uptake from 5.8 to 1.2 percent.

The decrease of 1.4 μg/dl blood lead, due to the lowering of water lead from 50 to 10 μg/l, is the same for each child subunit relationship as it is determined solely by the slope of the lines. In the rural low-intake situation (i.e., no pica), the drop of 1.4 μg/dl is a result of a decrease in percent contribution of water from 41.9 to 12.6.

8.2 Water-Lead-to-Blood-Lead Relationship in Pregnant Women

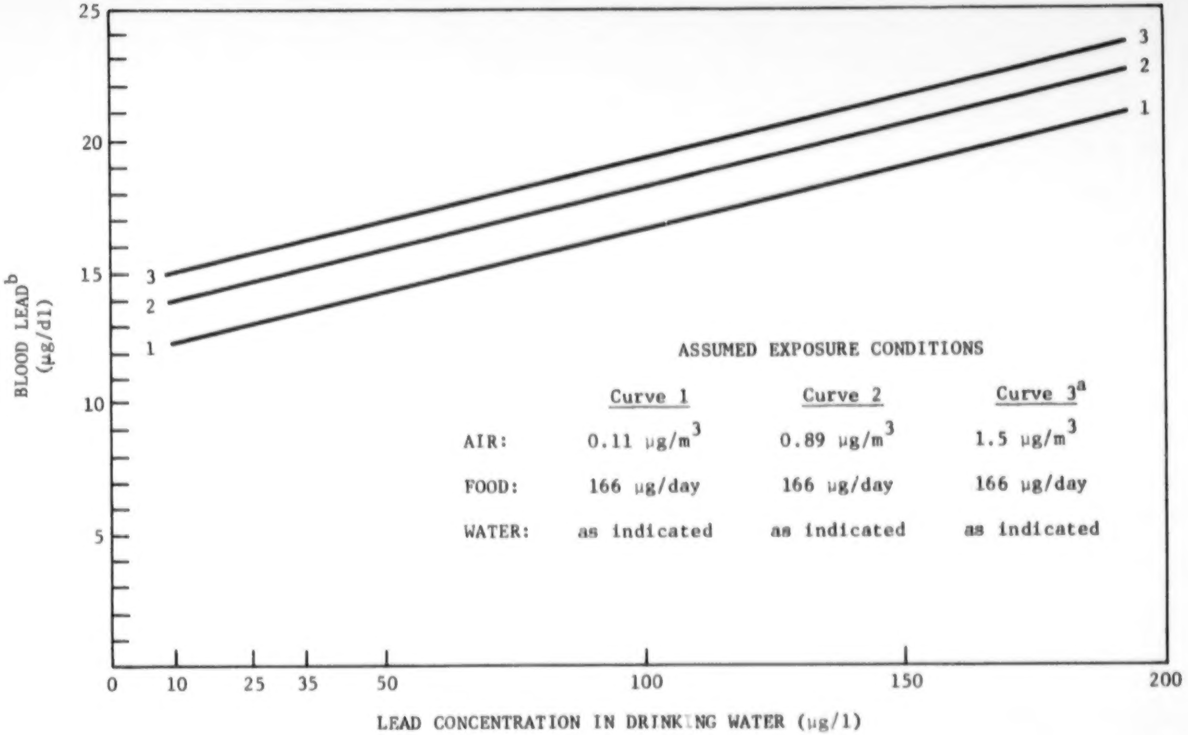
The combined use of the derived lead-uptake-to-blood-lead relationship and the source contribution model yield a water-lead-to-blood-lead straight-line relationship. Variations of lead concentrations in air are assumed to represent the rural-to-urban environmental gradient; while lead levels in food are assumed to remain relatively constant. Three air-lead concentrations were used to define the rural-to-urban gradient reflected in the total daily uptake value (Table 8-3). Using the derived uptake-to-blood-lead relationship, the blood-lead levels at these total daily uptake rates determined and were plotted against the varied water-lead concentrations (Figure 8-2).

TABLE 8-3

ESTIMATED DAILY LEAD UPTAKE AND BLOOD LEAD IN PREGNANT FEMALES

	RURAL		URBAN		AMBIENT AIR STANDARD	
[Pb] in Water	Total Daily Uptake (μg)*	Blood Lead (μg/dl)	Total Daily Uptake (μg)*	Blood Lead (μg/dl)	Total Daily Uptake (μg)*	Blood Lead (μg/dl)
10 μg/1	19.5	12.3	26.1	13.9	31.3	15.0
25 μg/1	22.5	13.0	29.1	14.6	34.3	15.7
50 μg/1	27.5	14.2	34.1	15.7	39.3	16.8
100 μg/1	37.5	16.6	44.1	18.1	49.3	19.2
200 μg/1	57.5	21.2	64.1	22.8	69.3	23.9

*See Table 6-5 for source contributions to total daily uptake



ASSUMED EXPOSURE CONDITIONS

	Curve 1	Curve 2	Curve 3[a]
AIR:	0.11 µg/m^3	0.89 µg/m^3	1.5 µg/m^3
FOOD:	166 µg/day	166 µg/day	166 µg/day
WATER:	as indicated	as indicated	as indicated

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[a] Air at ambient standard.

[b] Blood-lead levels calculated from total uptake, based on exposure conditions shown.

FIGURE 8-2
EFFECTS OF VARYING LEAD CONCENTRATIONS IN DRINKING WATER ON THE BLOOD-LEAD LEVELS OF A HYPOTHETICAL FEMALE ADULT

The three lines in Figure 8-2 illustrate the effect of increasing water-lead concentrations on three separate subgroups of the pregnant female population. It is apparent, as in Section 8.1, that the three lines share a common slope; thus they depict the same constant increase in blood lead over the exposure range of water lead. The total increase in blood lead over the range of 10 to 200 μg/l lead in water is 8.9 μg/dl, represented as a slope of 0.047. The y-intercepts are determined from the total uptake values computed by the source contribution model with water at zero, by their subsequent input into the derived-uptake-to-blood-lead relationship.

Although the fetus population has been identified as a sensitive group, urban pregnant women have blood lead values which vary only by 2.7 μg/dl (at the ambient air standard) from blood-lead values of pregnant rural women. The blood-lead level of these urban women at the current water standard is 16.8 μg/dl, well below the 30 μg/dl level set on by EPA and CDC as the level of undue lead absorption.

As presented in Table 8-3, the percent contribution of water to total lead uptake in pregnant urban women ranges from 6.4 percent (at 10 μg/l) to 25.5 percent at the standard (50 μg/l). Despite this percent contribution difference, the effect on blood lead of lowering the water-lead level from 50 to 10 μg/l is a decrease of only 1.8 μg/dl, a small fraction of the total blood lead.

8.3 Blood-Lead Contributions from Individual Sources

The straight-line relationships defined in this report between lead uptake and blood lead do not predict the expected blood-lead value of zero at a lead uptake of zero for either of the two sensitive populations considered. Perhaps this reflects significant deviations from linearity at low uptake values and the inability to accurately quantify all lead sources, especially at low levels. An implication of the nonzero intercepts is that an increase in lead uptake does not produce a proportionate increase in blood lead; for example, in the case of the urban pregnant woman (Table 8-2), with an air-lead concentration at the proposed standard, an increase in total daily uptake from 31.3 to 49.3 μg (58 percent) produces an increase in blood lead from 15 to 19.2 μg/dl (only 28 percent).

Assuming that subsequent to absorption lead taken up from the various environmental sources is indistinguishable to any physiological process it is possible to determine the blood-lead level attributable to any one source. This assumption implies that the percent contribution of a source to total lead uptake is equivalent to its percent contribution to blood lead. Source contribution factors can then be used to determine blood-lead levels resulting from individual sources. These source contribution factors are shown in Tables 8-1 through 8-3.

From data presented in these tables, it can be inferred that a constant uptake level from any one source does not contribute a constant amount of blood lead. Rather, a constant uptake may be responsible for different amounts of blood lead at different total uptake levels (as well as different percentages of the total blood lead). This effect is related to the nonzero y-intercepts of the lead-uptake-to-blood-lead relationships. In the pregnant female, with air lead at the proposed standard, there is a 58 percent increase in total lead uptake as lead in drinking water rises from 10 to 100 μg/l. A proportional increase in blood lead would lead to a value of 23.7 μg/dl; however, the defined relationship predicts a blood-lead level of 19.2 μg/dl, which is about 19 percent lower. Since uptake from the individual sources is indistinguishable, the blood lead attributable to each source will be 19 percent lower than that expected on the basis of proportional increase in uptake. For example, the uptakes from food and air remain constant (a proportional increase of 0 percent); therefore, the blood lead associated with these sources will decrease by about 19 percent. Uptake from drinking water increases from 2 to 20 μg/dl (900 percent); a proportional increase in blood lead due to drinking water would give a value of 9.6 μg/dl, and a 19 percent reduction in this value would give an actual blood-lead level due to water of 7.8 μg/dl.

9.0 CONCLUSION

The toxic effect of lead absorption is the cumulative result of exposure from many different sources. In order to define the toxicological impact associated with specific environmental lead-source concentrations, it is necessary to jointly consider all of the major exposure sources.

There are appreciable differences in exposure conditions between specific subsets of the population (e.g., adults vs. children, children with pica vs. children without pica, rural vs. urban populations) and these can be characterized by average exposure assumptions for the subpopulations in question. However, there is variability in the specific exposure conditions of individuals within these subpopulations which cannot be adequately quantified. The lead exposure of children with pica for paint is a striking example of this problem. Because of the wide variation in the lead concentrations in paint and existing painted surfaces, and the presumed wide range in rates of paint ingestion by children suffering from pica, the use of estimates of average paint-lead concentrations and consumption rates cannot reflect the diversity of blood-lead levels seen in these children.

This variability in exposure levels implies that there is considerable variability in the source contribution factors for all of the major environmental lead exposure sources. The significance of varying the maximum allowable concentration of lead in any medium, measured in terms of the ability to thereby modify the blood-lead levels of the population (or one or more sensitive populations), is a function of the total daily lead uptake and the source contribution factor for that medium. Therefore, the effect of a standard for that medium will not be uniform; rather, it will differ greatly between individuals.

9.1 Approach

If all sources of environmental lead are considered, the most effective means of reducing the overall blood-lead value of a given population can be determined. Utilization of the source contribution model provides the necessary data, since the percent contributions from various environmental sources and the total lead uptake at different environmental levels have been outlined. The model shows which environmental sources are most responsible for the given blood-lead level and thus identifies those areas in which regulatory action will have the greatest impact on blood-lead levels.

Large subsets of the population have been identified as being at a considerably higher risk from lead than the population as a whole. Therefore, it seems logical to approach the drinking-water lead standard from a sensitive population perspective. The standard can then be designed to directly benefit either or both of the sensitive populations, or a more sensitive subgroup (e.g., urban children, urban children with pica). Each of these options must be identified and discussed in terms of its impact on the final standard.

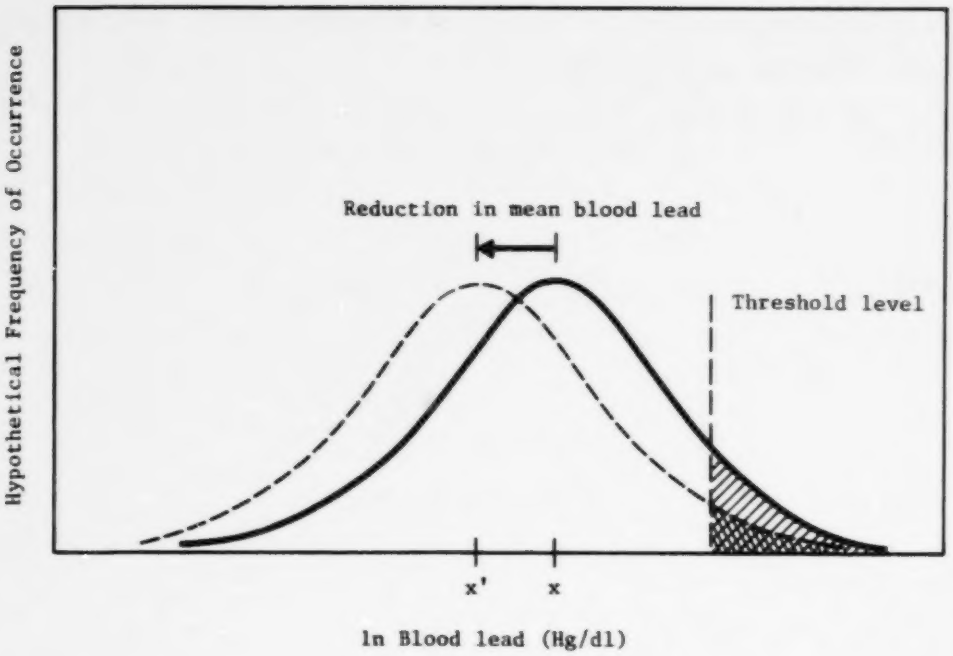
9.2 Effects of the Standard

The intent of any reduction in a standard for lead should be to lower the blood-lead levels of the exposed population, and in particular to reduce the blood-lead levels of those subgroups of the general population who have a greater risk of lead exposure (children) or who are more sensitive to lead than the rest of the population (fetuses and children). Since the American Pediatrics Association and the Center for Disease Control (CDC) have suggested that 30 μg Pb/dl blood is that threshold above which clinically significant adverse effects are noted in exposed children, it is prudent to assess the adequacy of the current standard in terms of the number of individuals whose blood lead falls above 30 μg/dl.

According to our results, lead-contaminated drinking water generally contributes a small fraction of the total daily lead uptake, and therefore will have only limited impact on blood lead. For example, a reduction of drinking water lead from 50 μg/l to 10 μg/l is expected to lower the mean blood lead of the hypothetical child population by about 1.5 μg/dl, or a pregnant female population's mean blood lead by 1.8 μg/dl. For high-risk youngsters (e.g., urban, inner city children with pica) with blood-lead levels approaching 35 or 40 μg/dl, the utility of a regulation that reduces blood lead by 1.5 μg/dl might be questioned. However, for the population as a whole, a reduction of 1.5 μg/dl in the mean blood-lead level can be substantial.

Blood-lead levels of U.S. children have been characterized as log-normally distributed, with a geometric standard deviation (GSD) of between 1.3 and 1.5 (EPA, 1978b). Given the 30 μg/dl threshold level, one can identify the percent of the exposed population with blood-lead levels below 30 μg/dl given a geometric mean blood-lead level. Or, if a selected percentage of the population is to be protected (as a safety margin), one can determine the particular geometric mean which will insure that that percentage will not exceed 30 μg/dl. In effect, this statistical treatment allows one to define the extent to which the "tail" of the frequency distribution exceeds a particular blood-lead level. A reduction in mean blood-lead levels of the childhood population, regardless of how small in relation to an individual's blood lead, can affect a significant portion of the total population by displacing the frequency distribution. Thus fewer individuals will exceed a defined threshold level (see Figure 9-1).

Using standard statistical methods applicable to log-normal distributions, one can calculate the mean (geometric) blood-lead level required if less than 99 percent of the observed population are to



▨ number of individuals with blood lead levels exceeding the threshold, given geometric mean of x

▧ number of individual with blood lead levels exceeding the threshold, given geometric mean of x'

FIGURE 9-1
EFFECT OF A REDUCTION IN MEAN BLOOD LEAD LEVELS ON THE NUMBER OF INDIVIDUALS EXCEEDING A THRESHOLD BLOOD LEAD LEVEL: LOG NORMAL DISTRIBUTION

have a blood-lead level less than 30 μg/dl. Assuming a geometric standard deviation of 1.4 (Angle and McIntire, 1978), and utilizing the following relationships:

$$\frac{\ln y - \ln M_g}{\ln S_g} = z \qquad (9\text{-}1)$$

and

$$F(z) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z} e^{-\frac{1}{2}u^2}\, du \qquad (9\text{-}2)$$

and

$$M_g = \frac{M}{e^{0.5 \ln^2 S_g}} \qquad (9\text{-}3)$$

where y = the CDC limit of 30 μg/dl
M_g = the geometric mean
S_g = the geometric standard deviation
z = a standardized random variable
F = fraction of the population with blood lead less than 30 μg/dl
M = the arithmetic mean

one can determine what fraction of the exposed population would have a blood-lead level less than 30 μg/dl, given various population mean blood-lead levels (see Figure 9-2).

Using the relationship in Figure 9-2, and the source contribution model discussed previously, one can determine the proportion of the sensitive subpopulations with blood-lead levels below 30 μg/dl as different control scenarios are applied to lead in drinking water. Tables 9-1 and 9-2 indicate those percentages (people with blood-lead less than 30 μg/dl) for the various subgroups of both identified sensitive groups.

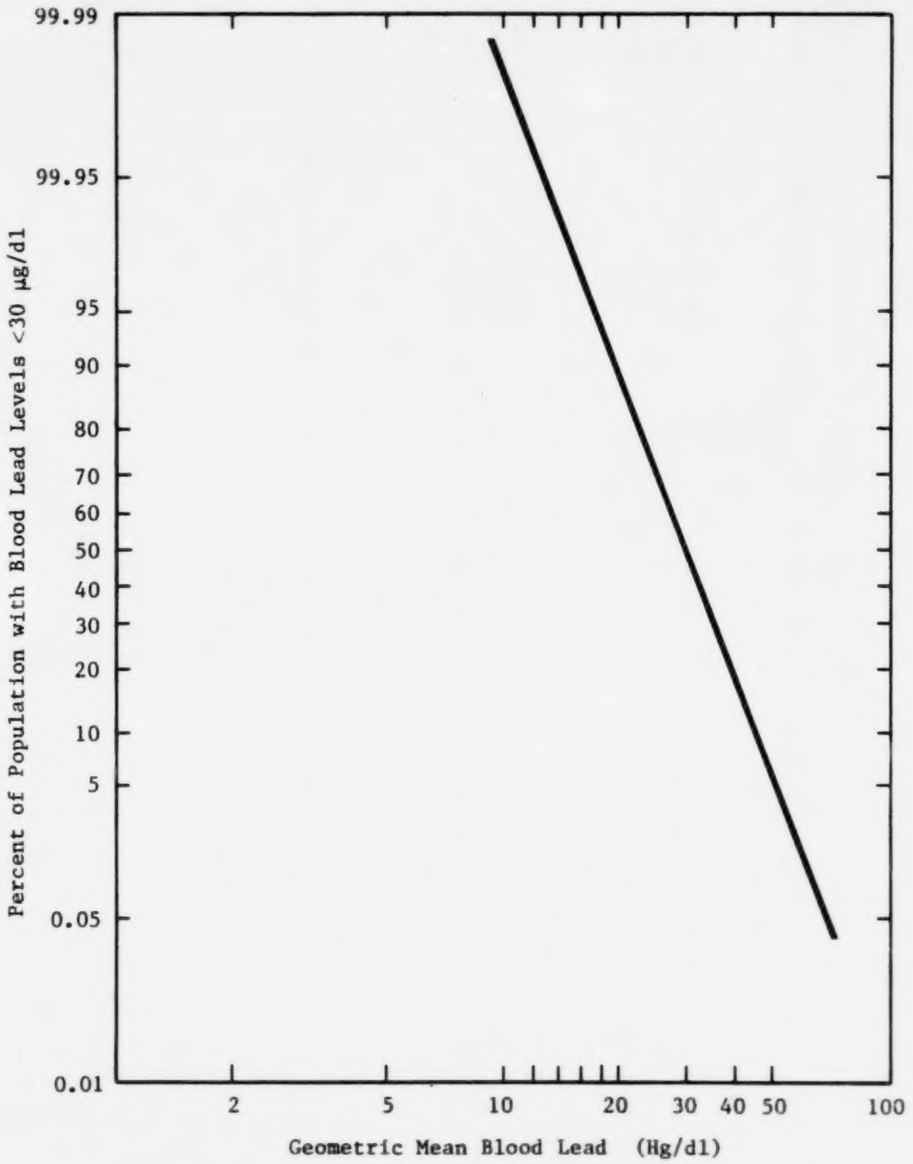


FIGURE 9-2
PERCENT OF CHILDHOOD POPULATION WITH A BLOOD LEAD LEVEL
≤30µg/dl FOR A SPECIFIED GEOMETRIC MEAN
BLOOD LEAD LEVEL (ASSUMING GEOMETRIC STANDARD
DEVIATION OF 1.4)

TABLE 9-1

SAFETY FACTORS ASSOCIATED WITH PROJECTED BLOOD-LEAD LEVELS FOR VARIOUS CHILD SUBPOPULATIONS[a]

	RURAL CHILD POPULATION		URBAN CHILD POPULATION[c]	
	Mean Blood Lead[b]	Population Below 30 μg/dl (%)	Mean Blood Lead[b]	Population Below 30 μg/dl (%)
Water @ 50 μg/l				
No pica	< 13.8 μg/dl	> 99	29.9 μg/dl	56.8
Pica w/paint @ 600 μg/g	< 13.8	> 99	30.7	53.9
Pica w/paint @ 8000 μg/g	22.7	83.9	40.3	11.4
Water @ 10 μg/l				
No pica	< 13.8	> 99	28.5	62.6
Pica w/paint @ 600 μg/g	< 13.8	> 99	29.2	59.9
Pica w/paint @ 8000 μg/g	21.2	88.7	38.8	15.5

---

[a] $s_g = 1.4$

[b] Arithmetic means as predicted by the source contribution/uptake to blood-lead model

[c] Air @ 1.5 g/m^3

TABLE 9-2

SAFETY FACTORS ASSOCIATED WITH PROJECTED BLOOD-LEAD LEVELS FOR VARIOUS PREGNANT FEMALE SUBPOPULATIONS[a]

	Mean Blood Lead[b]	Population Below 30 μg/dl (%)
RURAL (Air @ 0.11 $\mu g/m^3$)		
Water @ 50 μg/l	14.2 μg/dl	> 99
Water @ 10 μg/l	12.3	> 99
URBAN (Air @ 1.5 g/m^3)		
Water @ 50 μg/l	16.8	> 99
Water @ 10 μg/l	15.0	> 99

---

[a] s_g = 1.3

[b] Arithmetic means as predicted by the source contribution/uptake to blood-lead model.

More than 99 percent of rural children without pica, rural children with pica at low paint lead levels, and all female adults are expected to fall below the 30 μg/dl blood-lead guideline, given drinking water lead at the current interim standard of 50 μg/dl. Decreasing drinking water lead levels for these groups would have a negligible impact, since most individuals within those groups are already below the threshold. A larger proportion of the urban child population exceeds that 30 μg/dl blood-lead level; however, the drinking water contribution is only a small fraction of their total daily lead uptake. Assuming drinking water lead at 50 μg/l, between 43.2 and 88.6 percent of the urban child population is expected to have blood lead in excess of 30 μg/dl (see Table 9-1). By reducing the lead content of drinking water to 10 μg/l, between 37.4 and 84.5 percent would exceed the 30 μg/dl threshold.

The complete elimination of water lead from the uptake of the urban child yields mean blood-lead levels of 28.1, 28.9 and 38.4 μg/dl for children without pica, with pica at low paint-lead concentrations, and with pica at high paint-lead concentrations, respectively. The corresponding percentages of the population falling below 30 μg/dl are 64.1, 61.0 and 17.0, respectively. Therefore the total elimination of water lead in these groups adds 1.5 percent of the population to that portion already below the 30 μg/dl guideline.

The reduction of water-lead concentration does not appear to greatly affect the blood-lead distribution of the child population. However, an additional 6 to 7 percent of the population over the 30 μg/dl guideline will now fall within the "protected zone."

The effect of reducing the water-lead standard upon the fetus population is not clearly defined by the 30 μg/dl threshold criterion. It is apparent upon viewing Table 9-2 that water-lead reduction, although lowering the mean blood-lead level somewhat, has a negligible effect on the proportion of the adult female population below the 30 μg/dl level. The majority of the female adult population is at no no apparent hazard at the environmental concentrations considered. These blood-lead values (Table 9-2), although well below the threshold level, result in similar blood-lead levels in the newborn.

Since the fetus and the newborn are at substantial risk, it may be prudent to reduce the maternal blood-lead levels. For the adult female population, any change in lead levels in drinking water will have a proportionately large effect on blood-lead levels (due to the large source contribution factor), even though those blood-lead levels are already substantially below the 30 μg/dl threshold level.

Research Needs

Additional research is needed in several areas in order to properly evaluate the validity of the results obtained by using the source contribution model:

- Rates of intake of soil/dust and paint by children and the rates of absorption of the lead in these sources have not been adequately characterized.
- There are only limited data regarding host and environmental factors that affect lead intake, uptake and toxicity (e.g., age, nutritional status, hormonal status, chemical form).
- The toxicological differences between chronic and episodic exposures have not been properly evaluated.
- Comprehensive cost/risk/benefit analyses of all sources of lead exposure must be undertaken in order to determine the best overall regulatory approach.

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